

Mayo Magazine

SPRING 2007



Arizona oasis

New patient-care building opens


Mayo Clinic
Specialty
Building

ALSO INSIDE:

Improved techniques for viewing lung cancer
New therapy for inflammatory bowel diseases
Division of Engineering designs miracles
The extreme makeover of viruses

Mayo Magazine

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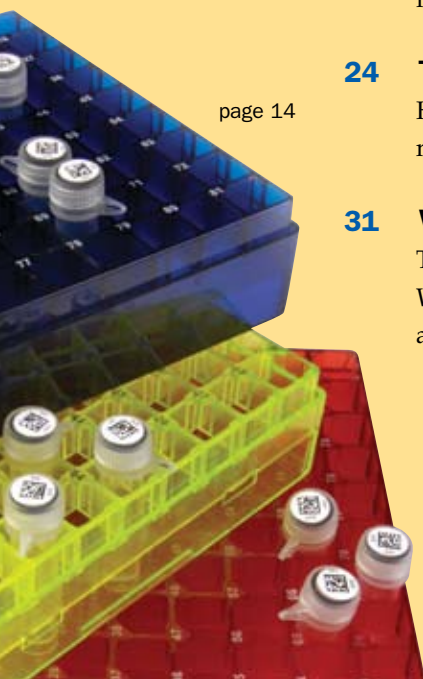
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A message from leadership

A BRIDGE TO THE FUTURE

Henry Plummer, M.D., a colleague of the Mayo brothers and a visionary in architecture and engineering, always emphasized that a medical building is a necessary tool of the physician in his or her daily work. With the recent opening of the Mayo Clinic Specialty Building (MCSB) in Arizona, our doctors, nurses and allied health staff now have a powerful tool to bring enhanced care to patients.

The MCSB stands next to Mayo Clinic Hospital on the Phoenix campus. The facility is equipped with state-of-the-art diagnostics and outpatient treatments, and its public spaces and exam areas are designed to create peace of mind, comfort and privacy for patients, their families and loved ones.

Many generous benefactors continue to join forces with Mayo Clinic in making the MCSB a reality. With their support, we are building a bridge to the future in Arizona. They are the true architects of Mayo's success in achieving its mission. It is my pleasure to introduce Christopher Beauchamp, M.D. As an orthopedic surgeon and chair of the committee that developed plans for the MCSB, he has been a strong advocate for this wonderful new facility.

Sincerely,



Denis A. Cortese, M.D.

President and Chief Executive Officer, Mayo Clinic



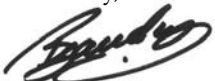
WELCOME TO THE MAYO CLINIC SPECIALTY BUILDING

I've been privileged to work on the steering committee for the Mayo Clinic Specialty Building in Arizona. Now my joy is to watch the building come to life, with patients and families and with all my colleagues doing what I firmly believe they do better than anyone else — provide the best care to every patient every day. Carl Pohlad, a longtime supporter of Mayo Clinic, once said, "When you walk in the door of Mayo Clinic, it's different from walking in anyplace else. It's what I call life pulsating."

Thanks to the firm foundation and guiding principles established a century ago by Drs. Will and Charlie Mayo, the institution has been able to successfully carry the Mayo Clinic Model of Care from Minnesota to Arizona and to Florida. No matter which Mayo Clinic door our patients enter, they are welcomed into a vibrant and compassionate world where hundreds of health care providers combine their energy to focus on the needs of the patient.

To take a tour, turn to page 2 for a glimpse of our new Mayo Clinic Specialty Building.

Sincerely,



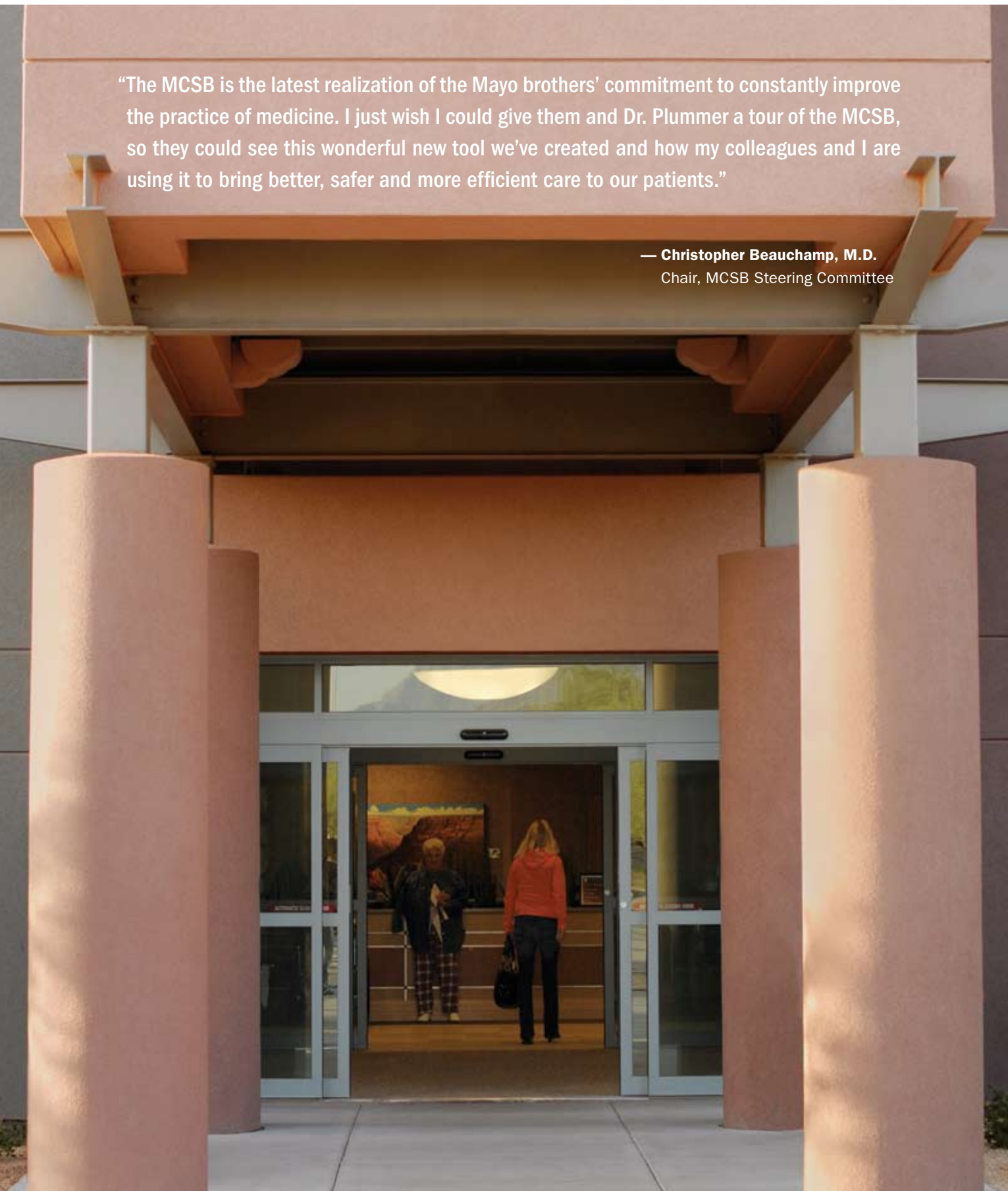
Christopher Beauchamp, M.D.

Chair, MCSB Steering Committee and Chair, Surgical Council



“The MCSB is the latest realization of the Mayo brothers’ commitment to constantly improve the practice of medicine. I just wish I could give them and Dr. Plummer a tour of the MCSB, so they could see this wonderful new tool we’ve created and how my colleagues and I are using it to bring better, safer and more efficient care to our patients.”

— **Christopher Beauchamp, M.D.**
Chair, MCSB Steering Committee



By Suzanne Winckler

A vision in the desert

Mayo Clinic Specialty Building takes shape

In 2000, a planning group at Mayo Clinic Arizona began to see the mirage of a new patient-care building standing next to Mayo Clinic Hospital on the Phoenix campus. The mirage might have been hazy at first, but the idea that inspired it was crystal clear. The Mayo Clinic Specialty Building, as it came to be called, would be the first step in Mayo Clinic Arizona's master plan to integrate and consolidate patient care on the Phoenix campus, and to create a collaborative biomedical research community on the Scottsdale campus.

As the facility evolved from mirage to blueprints to girders and beams, the planners — along with the physicians, nurses, technicians and administrators who would use the building — ensured that the building would provide improved communication between physicians and patients, state-of-the-art medical equipment and advanced Web-based systems to streamline the entire cycle of each patient's visit. Like all Mayo Clinic endeavors, it was a team effort driven by consensus.

"There was no single Renaissance person who provided all of the programmatic solutions for this project," explains Steven Pattyn, director of facility planning and design at Mayo Clinic Arizona. "It took the combined efforts of many Mayo resources and a lengthy series of design and operational meetings to pull this all together. It's impossible to design a complex building for health care without input from the people who are going to use it. One can't just make it up."

A work in progress

Work began on the Mayo Clinic Specialty Building (MCSB) in 2004. A Webcam, linked to Mayo Clinic internal and external Web sites, allowed employees and the public to watch the building take shape.

Christopher Hilgemann, MCSB project manager, seldom seen without his hard hat, sent updates to key staff containing the kind of details that would awe the weekend

home-repair hobbyist: "... 95 percent completed with interior metal stud wall framing on the concourse Radiation Oncology floor ... ductwork, plumbing and electrical work is very active on concourse ... installation of Radiation Oncology's new linear accelerator on schedule for January ... completed pouring the Healing Garden concrete retaining walls."

The Healing Garden especially became a labor of love for project planners. Located on the concourse level by the Radiation Oncology Department, it is open to all patients and visitors, but is especially accessible to patients undergoing radiation therapy for cancer. The Healing Garden is a special expression of Mayo Clinic's Humanities in Medicine Program, which is devoted to integrating art, music and compassionate design into the medical environment.

In 2005, Mayo Clinic Arizona began collaborating with four Native American artists affiliated with the Heard Museum of Native Cultures and Art in Phoenix. The artists designed 10 mosaic benches for the Healing Garden using themes suggested during talks with Mayo Clinic staff and patients. More than a dozen benefactors stepped up to support the project. The benches incorporate many curative and life-affirming Native American motifs (seen above), such as dragonflies, the sun and landscape. The benches are grouped to create intimate spaces within the Healing Garden. "Illness is exhausting for all concerned. The way the benches are placed allows you to take a breath," says Connie Tsosie Gaussoin, one of the artists.



From special lights to a special beam

Early in the 20th century, Henry Plummer, M.D., Mayo Clinic's renowned efficiency expert, designed the first wall-lighting system to track exam-room occupancy. The tier of lights outside each exam room, a hallmark of Mayo Clinic, has evolved over time to incorporate new technologies. As part of the MCSB planning, a team of cabling and computer experts, headed by Rocky Fransen, has raised the science of room occupancy to a new level.

Mayo Clinic's first Web-based room-occupancy system tracks each patient on an interactive program used by registration, nurses and physicians. The program, which triggers lights outside each exam room, follows the patient from the time a room is reserved (purple light), to occupancy (white), through the exam with nurses and physicians (yellow, orange and blue), to a signal requesting the room be prepared for the next patient (purple and orange).

The system records the time patients spend in rooms prior to their exams. This information is analyzed to ensure wait times are kept to a minimum. The system, however, does not track the time a patient spends with a physician, underscoring Mayo Clinic's promise to physician and patient alike that there will always be enough time to conduct a thorough exam.

It took more than a year to work out the program and design the lighting system to get the "splash" (how the lights reflect off the wall) and color of the LED lights just right.

The MCSB is a product of infinite details and a work of profound generosity. It is being funded almost entirely by benefactors, who have so far contributed about \$34 million toward the project. In February 2005, many of these generous supporters, as well as Mayo Clinic patients and employees, had the opportunity to write personal notes on an 800-pound, 20-foot-long steel beam. It took 12 strong employees to carry the beam into and out of Mayo Clinic on the Scottsdale campus. Some of the inscriptions included, "Cancer clean after 5.5 years. Thanks Mayo." ... "Thanks, Mayo, for my leg."

Five months later, with completion of the structural steel frame for the MCSB, construction workers raised this special beam to the roof of the building as part of a traditional "topping off" ceremony and decorated it, as is the custom, with a tree and the American flag.

The commemorative beam is just one of countless examples of the care and planning that have gone into the MCSB. Every beam and girder, switch, cable, socket, doorknob and exam-room light tells a story of choices made with one, and only one, goal in mind — assuring that the needs of the patient come first. ■

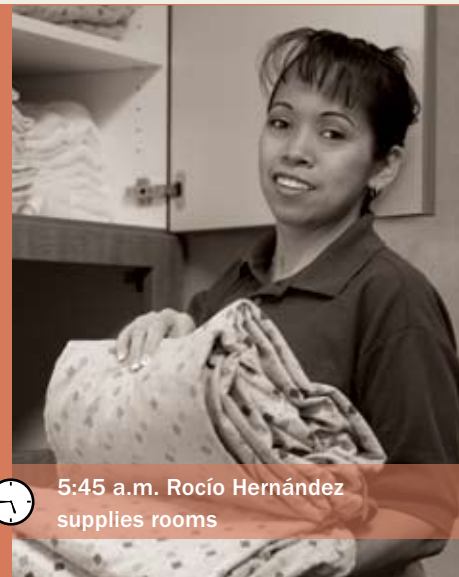
A day in the life ...

Mayo Clinic Specialty Building (MCSB) is the first step in Mayo Clinic Arizona's master plan to integrate and consolidate patient care on the Phoenix campus, and to create a collaborative biomedical research community on the Scottsdale campus.

Here is a
daylong
look at the
happenings
inside the
Mayo Clinic
Specialty
Building



5:45 a.m. Rocío Hernández
supplies rooms



5:45 a.m. Rocío Hernández has been at work since 4 a.m. She is wending quietly through the corridors of the Mayo Clinic Specialty Building (MCSB), pushing a cart stacked with patient gowns and checking each exam room to make sure the linen closets are well supplied for the day. As part of its commitment to patients, Mayo Clinic provides soft cotton gowns, rather than those stiff disposable ones that make a patient feel like a life-sized paper doll. Ms. Hernández and her 130 colleagues in

Building Services keep Mayo Clinic facilities well provisioned and neat as a pin. As Todd Thyssen, the MCSB/Mayo Clinic Hospital housekeeping manager, says, “Just try to find a speck of dust in this building.”

8:05 a.m. It’s a chilly morning — for Arizona — and General Service attendant Brian McIntosh stands at his post at the entrance of the MCSB with a warm smile and a helping hand. He ushers patients into the building with the skill of a traffic cop and the kindness of a Samaritan. “Good morning.” “May I get you a wheelchair?” “Have a nice day.” “If you’ll wait a moment, I can order an electric cart to give you a lift over to the hospital.” “Let’s see, you just need to take the elevators to the concourse level.” “The restrooms are to your right.” “Yes, it sure is nippy, but it’ll warm up soon.” Mr. McIntosh is living proof that Mayo Clinic’s promise — the needs of the patient always come first — begins right at the front door.

J. Harsha, M.D., a fellow in advanced head and neck surgery, will check the progress of Cecilia Monarque. Dr. Hayden and his team replaced her jawbone, which had been fractured by a tumor, using a piece of bone and associated artery and vein from her leg. Not a hint in Ms. Monarque’s countenance suggests her surgical reconstruction. The next step is to provide her with dental implants so, as Dr. Hayden says, “She can bite apples and chew steak.”

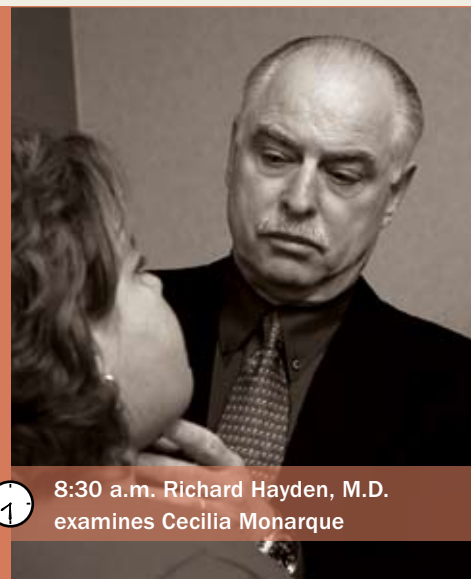
9:35 a.m. “We are thrilled with our new area,” says hand therapist Cynthia Ivy. “It’s 30 percent larger, with a private whirlpool room, more privacy at the patient stations and closer proximity to the doctors.” Opened barely two weeks, the Hand Therapy Suite is packed this morning. At all eight stations, hand therapists are literally holding their patients’ hands, gently massaging, bending and flexing fingers and thumbs. Everyone is talking quietly, and there’s a sense



 8:05 a.m. Brian McIntosh (left) greets patients

“It’s impossible to design a complex building for health care without input from the people who are going to use it.”

— Steve Pattyn



 8:30 a.m. Richard Hayden, M.D. examines Cecilia Monarque

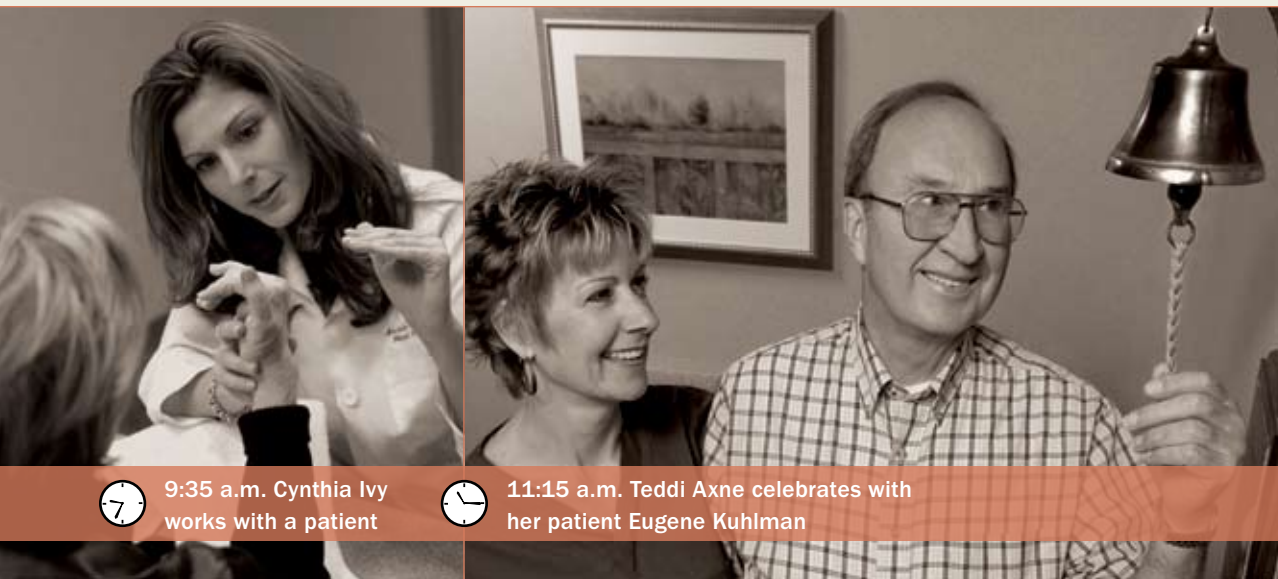
8:30 a.m. “Since moving into this new facility, we can truly provide our patients with one-stop shopping,” says head and neck surgeon Richard Hayden, M.D. He and his colleagues across all surgical specialties can make better use of their time in surgery and time spent with patients because the MCSB provides 133 patient exam rooms right next door to Mayo Clinic Hospital. Pre-MCSB, surgeons and patients alike had to drive between the Scottsdale and Phoenix campuses. While they see patients this morning, Dr. Hayden and Wayne

of deep concentration throughout the room. The hand is a beautiful and complex instrument that people take for granted until it malfunctions. Maureen Silhasek suffers from rheumatoid arthritis. Hand therapist Michelle Smith adjusts a made-to-order splint that Mrs. Silhasek has been wearing after surgery to improve mobility and dexterity of her right hand. Mrs. Silhasek does a series of exercises while Ms. Smith measures. “You’ve got a 5 percent increased extension in one finger and 2 percent in the other,” she says. “That’s excellent.”

11:15 a.m. Eugene Kuhlman has a big grin on his face, and for good reason. He's just completed his eight-week course of cancer radiation therapy, and he's ringing the bell that hangs on the wall in the new Radiation Oncology patient area just for this celebratory purpose. His therapist, Teddi Axne, celebrates with him, and there is a round of applause from fellow patients who are awaiting their treatment — and the time when their turn comes to ring the bell. At 30,000 square feet, the new Radiation Oncology Department in the MCSB is two and a half times bigger than the patient area on the Scottsdale campus. Mayo Clinic can now treat an additional 60 to 65 cancer patients a day. Chris Bernard, another radiation therapist responsible for Mr. Kuhlman's care, says the new space helps him better care for patients. "The interior design is very logical and enhances the flow of patients, and it's very tranquil," he says.

colorful desert landscapes. Susan King, one of five patient services representatives in the MCSB, prepares for the stream of patients coming in for appointments after the noon lull. Among the many attributes that recommend Ms. King for this job is her beautiful smile. "Hi, there," she says to a patient who has stepped up to her desk. After determining the patient's name and pulling up her medical record on the computer, Ms. King says, as if this were the first, not the jillionth time today she has asked this question, "Can you tell me your birth date, please?" She surrounds the patient with a sense of caring and concern, and in her warm, efficient manner she helps bring the building's design to life.

3:15 p.m. Lyndsay Russell, R.N., is the living donor coordinator for liver transplantation at Mayo Clinic Arizona. She counsels people who volunteer to give part of their liver



9:35 a.m. Cynthia Ivy works with a patient



11:15 a.m. Teddi Axne celebrates with her patient Eugene Kuhlman

"All our design decisions focus on patients and making sure they feel welcome, secure and comfortable."

— Steve Pattyn

1:20 p.m. "All our design decisions focus on patients and making sure they feel welcome, secure and comfortable," says Steve Pattyn, who guided the design for the MCSB. As with all Mayo Clinic facilities, a priority design issue for him and the planning team was way-finding — making sure patients can easily navigate through their round of appointments in the building. The first panorama patients see when entering the MCSB is a brightly lit bank of registration desks trimmed in warm wood. On the walls are murals of

to a relative or friend who will not survive without a liver transplant. Mayo Clinic Arizona ranks No. 1 in the state and seventh in the nation in performing this procedure. Ms. Russell is very pleased with the new transplantation area in the MCSB. "There's more privacy for our patients and more space," she says. "We can see more patients in a day, and we have room to grow." Ms. Russell's job is to educate the potential organ donor. She methodically explains the risks of the surgery and the postoperative recovery period

while the living donor's own liver regenerates. She prepares prospective donors for five days of medical tests to check their health and determine if they qualify. If tests reveal that a prospective donor is not a good match, Ms. Russell will explain why — a delicate task that draws upon her abundant compassion. She spends all the time it takes — usually about an hour and a half — in her first encounter with a living donor. Besides her role as educator, she puts people at ease and underscores their generosity. "You are offering a gift," she says to a prospective donor. "I'm here to be your advocate in the process. Your safety is my first priority."

4:30 p.m. The Healing Garden is in cool shadows. Walter Heilman sits on a bench quietly reading. The sound of water offers a soothing background. Pavers scattered on the garden's floor are inscribed with "Peace" and "Hope"

affiliated with the Heard Museum of Native Cultures and Art in Phoenix. The artists designed the 10 benches in the Healing Garden, using themes suggested during meetings with Mayo Clinic staff and patients. Each mosaic bench incorporates a motif or symbol special to the artist's culture and traditions. These include images of dragonflies, rivers, corn, the sun and moon. "My hope is that these benches evoke feelings of strength, healing, nourishment and balance," says one artist, David Gaussoin, who is of Picuris, Navajo and French heritage. ■

For information about the MCSB, please visit www.mayoclinic.org/mayo-magazine.



 1:20 p.m. Susan King greets a patient



 3:15 p.m. Lyndsay Russell, R.N. counsels a patient



 4:30 p.m. Walter Heilman, a patient at Mayo Clinic Arizona, relaxes in the Healing Garden

and "Courage." The Healing Garden at the MCSB is on the concourse level next to Radiation Oncology. Placed below ground on the building's northeast side, it is a cool, inviting space even in the high heat of the Arizona summer. Intimate seating areas are clustered throughout the garden. This place is living proof of Mayo Clinic's commitment to provide environments that promote healing. To embrace the many life-giving symbols of the Native American cultures of the Southwest, Mayo Clinic collaborated with four artists

The MCSB is a product of infinite details and a work of profound generosity. It is being funded almost entirely by benefactors who have contributed about \$34 million toward the project.

2 doctors + 2 instruments

Equal effort improves lung cancer staging

A simple maxim helps define the Mayo Clinic Model of Care: Two (sometimes more) heads are better than one for treating patients. At Mayo Clinic Jacksonville, researchers have coupled this philosophy with advanced technologies to discover that two high-tech endoscopes are better than one round of surgery, the traditional approach, to diagnose the spread of lung cancer. In fact, the combination of the two scopes is almost perfect, according to recently published research.

The point system

Staging, a four-point scoring system that physicians use to determine the extent to which cancer has spread, is the most important variable in treatment decisions and prognosis for lung cancer. Physicians assign scores based on tissue samples taken from masses in the lung and surrounding lymph nodes. Patients with stages 1 or 2 are generally treated with surgery. The majority of stage 3 and stage 4 patients are treated with chemotherapy and/or radiation.

Determining a cancer's stage is vital to providing the right treatment; however, accurate lung cancer staging has been difficult until recently.

Two instruments, better results

Led by Michael Wallace, M.D., a gastroenterologist, the Jacksonville team has developed a combined technique that uses two types of endoscopes to stage lung cancers. The procedure takes about two hours, requires only a mild sedative and patients go home the same day. Even better, it's highly accurate and, to date, complication-free, Dr. Wallace says.

"We've used this technique on more than 150 patients; it's accurate 97 percent of the time, and so far we've seen no complications," Dr. Wallace says.

Prior to using the combined technique, the best way to stage lung cancer tumors was surgical biopsy of lymph nodes in the chest — the first place lung cancer tumors spread after they leave the lungs. But trying to stage lung cancer by surgical means is accurate only about 50 percent of the time. Also, the procedure requires general anesthesia and can sometimes result in an overnight hospital stay.

Collaborating for a clearer view

Prior to joining Mayo Clinic in 2002, Dr. Wallace conducted extensive research at the University of South Carolina on endoscopic ultrasound (EUS), a flexible tube with an ultrasound probe and a very thin needle.

Through their experiences, Dr. Wallace and colleagues noted that the newer equipment allowed them to clearly see the lymph nodes behind the lungs, which sparked an idea: perhaps the technology could be used for lung cancer staging.

The chance to better explore that possibility lured him to Mayo Clinic, Dr. Wallace says. Because of Mayo's reputation for collaboration, he would have the opportunity to work with lung specialists and surgeons to determine if the equipment would help improve lung cancer staging.

"The biggest barrier to this type of research is the fact that most institutions don't encourage collaboration among physicians," Dr. Wallace says.

Shortly after his arrival, Dr. Wallace had the opportunity to put Mayo's collaborative environment to use. Olympus



Jorge Pascual, M.D., and Michael Wallace, M.D.

“This experience really exemplifies what Mayo is all about. It is combining everything we do — patient care, education and research — and it increases the quality of patient care.”

— Jorge Pascual, M.D.

“We’ve used this technique on more than 150 patients; it’s accurate 97 percent of the time, and so far we’ve seen no complications.”

— Michael Wallace, M.D.

Corporation asked him if Mayo would consider testing a new type of ultrasound probe, called an endobronchial ultrasound probe (EBUS). Essentially a smaller version of the EUS probe, it was designed for pulmonologists, who use the probe to explore the lungs.

As they tested the equipment, Dr. Wallace and Jorge Pascual, M.D., a pulmonologist at Mayo Clinic Jacksonville, realized that EBUS provided excellent views of the lymph

nodes in front and on either side of the lung. From there a match was made, Dr. Pascual says.

“With the EUS, we knew we could see behind the lung, but with the EBUS we could see the sides and front, so the two scopes together would give us the ability to see everything we needed to see to accurately determine the stage of lung cancer,” he says.

Study benefits patients

Funding from the National Cancer Institute and Olympus enabled Drs. Wallace and Pascual, as well as cardiothoracic surgeon John Odell, M.D., to begin a large research study to evaluate the effectiveness of lung cancer staging techniques. They looked at EBUS, EBUS plus EUS, and surgical biopsy. Their study is the only one in the United States to compare these techniques, and it is the largest study of its kind in the world.

Together, EBUS and EUS proved more accurate than surgery, and the combination of the two devices was 97 percent accurate in determining the stage of lung cancer. In creating a test with such a high degree of accuracy, the team is saving patients from unnecessary surgeries, says Dr. Odell.

"This helps us avoid a scenario where we find out on the operating table that a patient has a tumor that has spread beyond the lung," Dr. Odell says. "These patients don't benefit from surgery, in terms of producing a cure for the disease, and yet they're still exposed to all the risks and complications that go along with surgery."

Passing on knowledge

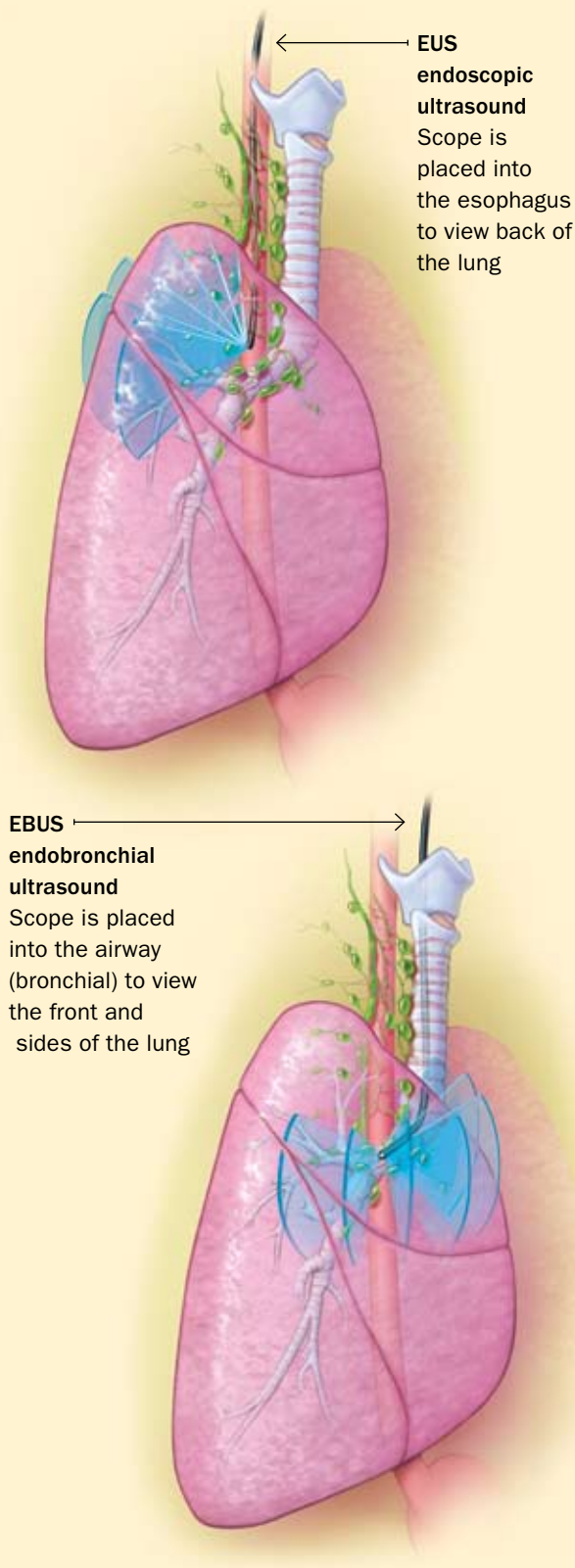
At Mayo Clinic Jacksonville, the combination of EBUS and EUS has become the standard technique for staging lung cancer. Drs. Pascual and Wallace say their immediate focus is to educate other physicians on the technique. They have begun training their Mayo colleagues, and they're also receiving requests from physicians at other institutions to observe the technique.

The Mayo team also wants to perform additional research to expand the use of the equipment. One scenario they want to investigate is its use for re-staging of lung cancer. Patients have computerized tomography (CT) scans to assess their response to chemotherapy or radiation therapy for the disease, but these scans offer only limited views of the lungs, Dr. Wallace says. EBUS and EUS could be used to determine if the cancer was still outside the lungs and could indicate to physicians how well the patient was responding to therapy.

"This experience really exemplifies what Mayo is all about," says Dr. Pascual. "It is combining everything we do — patient care, education and research — and it increases the quality of patient care." ■

An improved view of lungs

Combination of ultrasound techniques improves viewing and staging of lung cancers



By Michelle Felten

Inflammatory bowel disease

Heroic patients and determined doctor work toward a cure

For more than 1 million Americans, the diagnosis of inflammatory bowel disease (IBD) is much more than a disease classification; it's an unpleasant reality and a way of life.

For William Sandborn, M.D., a gastroenterologist at Mayo Clinic Rochester, finding a treatment and eventually a cure for IBD is one of his life's goals. And he thinks he's onto something with biologic therapy, a new and sometimes experimental therapy for conditions such as ulcerative colitis and Crohn's disease, two of the most common inflammatory bowel diseases.

Biologic therapy primer

In the broadest sense of the term, biologic therapy uses living organisms or cells to make proteins or hormones. Then, in something resembling the ultimate recycling program, the proteins are administered to another living organism as a medication, often targeting the body's immune system to reduce symptoms. Obviously, the process involves much more than simply extracting protein secretions from one organism and injecting them into another, but this is the basic concept behind biologic therapy.

Dr. Sandborn, a clinical researcher who directs the Inflammatory Bowel Disease Interest Group in the Division of Gastroenterology and Hepatology, spends much of his time testing potential biologic therapy drugs as he designs and conducts clinical drug trials in the hope of one day curing IBD. He does it for his patients.

"People who participate in clinical trials are heroes," says Dr. Sandborn. "They go the extra mile. It's a largely selfless act, a civic act of testing new drugs in an effort to help us find new treatments."



William Sandborn, M.D.

"I'd say there are approximately 50 biotechnology companies that are currently developing new treatments for IBD, and there has been more and more interest in the area of IBD over the past 10 years," he says. "I'm hopeful that one of these new medications will prove to be the cure, but at the very least, I know some of these agents will offer better and safer treatments for our patients." At any given time, Dr. Sandborn and his team are involved in 10 to 20 such multicenter clinical trials, testing new drug treatments almost as quickly as they're produced.

The anatomy of a disease

IBD, a disease that's usually diagnosed in a person's teens and early 20s, often means a lifetime of misery for those who have it. Ongoing bouts of inflammation of the digestive tract lead to abdominal pain and severe bouts of watery or bloody diarrhea, which make the disease impossible to ignore and challenging to live with.

Here's how the disease manifests: As part of the immune response, the body naturally produces the protein TNF-alpha. This protein's job is to signal your white blood cells to step up efforts to fight infection when it's present. This all-out white blood cell war temporarily causes inflammation in the affected area. Normally, the body gets rid of this excess protein after the threat of infection has passed, but for people with inflammatory bowel diseases, this protein protector isn't sloughed off. Instead, the protein keeps signaling to supply more white blood cells. This vicious cycle eventually causes the protein to build up, leading to excessive inflammation, pain, tissue damage and the uncomfortable and often unpredictable diarrhea.

The anatomy of a therapy

Biologic therapy works to halt this vicious cycle at its roots, the molecular level. Here's how it works: To produce medications that keep the TNF-alpha protein under control, the first step is to create antibodies, or protection, against it. This process is similar to the steps that go into creating vaccines. Vaccines for viruses such as mumps, measles and chicken pox are created by giving people small, measured doses of the virus itself so the body can build up antibodies, or a defense, against it. That way, a defense system is in place the next time the body encounters the virus.

The process is the same for creating TNF-alpha inhibitor medications. When a small number of mice are injected with this human protein, the mouse's body creates antibodies against it. The mouse antibodies are then genetically engineered to create an antibody that's partly mouse and partly human. In some instances, human genes that make antibodies are genetically inserted into mice so that when the mouse is injected with a human TNF protein, it is already

making the proper human antibody. The reason is simple: The body is much more likely to accept something it recognizes, lessening the rate of side effects sometimes seen in mouse-produced antibodies.

Once a gene has been created that makes a partly or fully human antibody to TNF, it's inserted into cultures of cells such as the Chinese Hamster Ovary (CHO) cell line or another small living organism such as *E. coli* bacteria that can be grown in large sterile vats to mass produce the antibody for use as a medication in humans.

The TNF-alpha inhibitor medications create almost miraculous results for many, freeing them from ongoing IBD symptoms and allowing them to lead normal lives for the first time in years. And although the experimental therapy involves intravenous infusion of biologic therapy for about two hours once every eight weeks, the time spent in the infusion room is well worth it for many.

One-dose therapy, soon?

"We are nearly at the point of having a medication that could be self-administered at home," says Dr. Sandborn. "It will be a tremendous time saver for our patients. And it would be great if someday we could find a biologic agent that was a one-dose curative therapy. Right now the biologic agents that we're using only put the disease into remission. So we're currently at the stage of being able to offer a suppressive, not a curative, therapy for patients. We're just not to the point of a permanent, quick fix for this disease. Not yet.

"Biologic therapy is pretty much a lifetime commitment for patients. We find that when we discontinue the medication, as many as 80 percent of people have a relapse of their symptoms. And when we stop and restart the treatment, we see that the therapy is not as effective the second time around. Long-term treatment is just much more effective than intermittent dosing for this type of medication, unfortunately. But I know there's a better treatment out there. We just have to find it." ■

For information about inflammatory bowel diseases, please visit www.mayoclinic.org/mayo-magazine.

Experimental therapy relieves burden of Crohn's disease

Richard Johannsen's passion is robotics technology. His burden is Crohn's disease, a painful and debilitating condition that causes chronic inflammation of the digestive tract. Diagnosed in his 20s, he underwent so many small bowel resections that further surgery would put him at risk for malabsorption of nutrients.

Since becoming a Mayo Clinic patient in 1997, Mr. Johannsen has never looked back. Though he is not about to go off and conquer Rome, his figurative crossing of the Rubicon River in Nevada has allowed him to renew his passion.

Recently, Mr. Johannsen built a full-sized, remote-controlled 4x4 vehicle to race in the Defense Advanced Research Projects Agency (DARPA) Grand Challenge — a field test in the Mojave Desert. DARPA, the research arm of the U.S. Department of Defense, develops remote-controlled vehicles to save lives on the battlefield. The race allows inventors to contribute ideas. Mr. Johannsen was able to participate because the clinical research conducted by William Sandborn, M.D., gave him access to therapies that relieved his symptoms.

"Coming to Mayo turned my life around," says Mr. Johannsen. "Before coming here, I couldn't even get out of bed. It's a miserable disease that affects every aspect of your life. Now my disease is in remission."

Helping patients return from a personal hell

Dr. Sandborn, a gastroenterologist and clinical researcher who directs the Inflammatory Bowel Disease (IBD) Interest Group in the Division of Gastroenterology and Hepatology, helps patients return from the personal hell caused by IBDs. Although the disease is not considered deadly, people who have IBDs frequently feel so wretched that death sometimes seems a welcome release. That's why Dr. Sandborn is excited by the knowledge that his research has contributed to an array of new treatments.

"I spend much of my time designing and administering multicenter trials," says Dr. Sandborn. His primary focus is on biotechnology therapies. "The new biologics suppress these diseases for long periods of time without massive doses of steroids or disabling surgeries."

Mr. Johannsen is reaping the benefits of the latest biotechnology for Crohn's disease.



Richard Johannsen

The first of the biotechnology agents

"Mr. Johannsen came to us with a fistula in his lower rectum — a common problem for people with Crohn's disease," explains Dr. Sandborn. "Our surgeons were able to close the fistula without major surgery. We then started him on Remicade. It was the first biotechnology agent available for the treatment of patients with Crohn's disease."

"However, some patients develop antibodies to the mouse protein in Remicade, which causes side effects."

Unfortunately for Mr. Johannsen, he was one of those people, so his best hope was with experimental therapies.

In December 2002, Humira, another medication, was approved by the Food and Drug Administration for the treatment of rheumatoid arthritis.

Dr. Sandborn was excited that this may be just what Mr. Johannsen needed because it was a human protein that resembles antibodies normally found in the body.

In November 2003, Mr. Johannsen began participating in Dr. Sandborn's clinical trial to show Humira's long-term effectiveness. That's when he really started to feel great.

"To learn about the challenges my robotic vehicle would face, I had to drive four days in a conventional 4x4 over the Rubicon Trail — that's an extreme track in Nevada that crosses the Rubicon River. I never could have even thought about attempting that before," says Mr. Johannsen. "I feel blessed to have found Mayo where people look after my best interests." ■

By Michelle Felten

DESIGNING miracles

Engineers solve problems to improve patient care

The certificate in his office reads: Geek of the Week. The laminated proclamation shares office space with his Massachusetts Institute of Technology (MIT) and Harvard diplomas and is as prominently displayed as other honors he's received in his 30 years as an engineer. Kevin Bennet is proud of his geek status, as are the other 53 members of the Mayo Clinic Division of Engineering and Technical Services. And they have reason to be proud.

Every day, these engineers — biomedical, electrical, software, mechanical and chemical — work on inventions to make doctors' jobs easier and patients' lives better.

"Our job is to find the miracle," says Mr. Bennet. "When a doctor or researcher comes to the Division of Engineering and asks us to build a device or design a software program to solve a problem, we immediately look for the miracle that needs to occur. We ask ourselves: What's the unique aspect of the problem that needs to be solved in order for us to build this device or design that software? Once we've answered that question, we work to make it happen."

Step by step by step

The process is fairly simple, although the steps leading to the solution may not be, says Mr. Bennet, chair of the division.

Whether it's figuring out a way to better retrieve one of 100,000 vials in a busy research lab, or designing a finite surgical tool to allow surgeons to work on the heart's mitral valve without opening the heart, or redesigning infrastructure to help reduce noise in patient-care areas, the engineering team is on it.

"When a request comes in, we look at the problem with the doctor or researcher, create some definition of the issues and brainstorm possible solutions," says Mr. Bennet. "Sometimes the doctor or researcher comes with a developed solution; sometimes they just come with a problem. After that

discussion, we take a look at our various teams of engineers to decide which groups are best equipped to develop the answer. We handpick people within each engineering group to work on the project. We all have specific areas of interest and expertise, so we always try to match the problem with the people who have the skills to attack that problem." Next is the often-painful part.

Doing their homework

"Everyone always wants to jump right in and start soldering stuff together. Building it is the fun part. But if you rush into it, you'll end up with something that won't work and won't solve the problem it was intended to solve, so we take the time to do our homework," says Mr. Bennet.

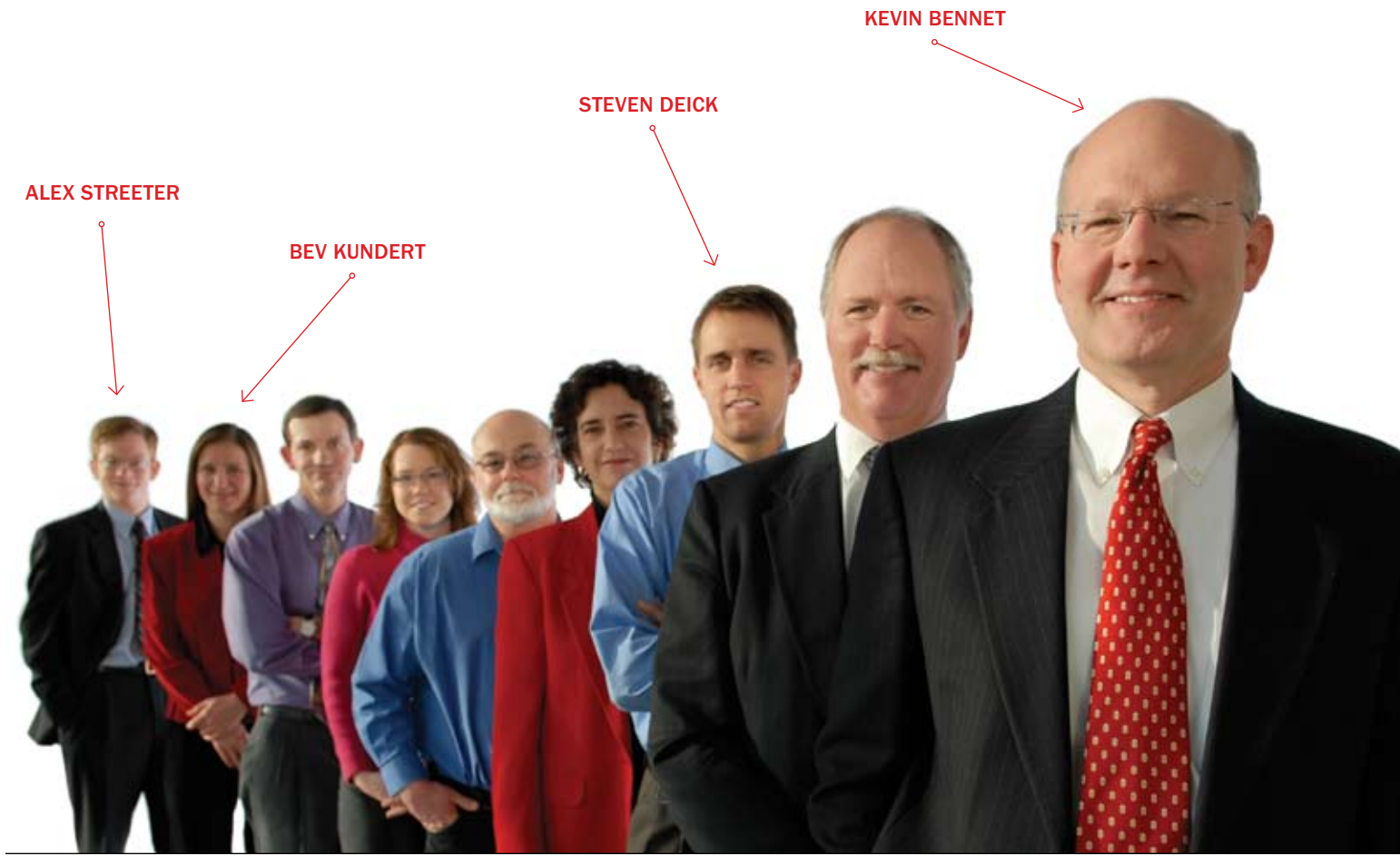
Engineers may spend hours in research labs or in patient-care areas studying processes and interviewing people. And depending on the project, they also may conduct extensive background research on similar projects or devices to learn how those devices succeeded and failed. They determine which roads have already been traveled.

"The homework phase of any project can be painstaking, but if we don't take the time upfront, we can't deliver the right solution," explains Mr. Bennet. He emphasizes that sometimes the right solution is to give the requestors what they need rather than what they asked for. The difference is much more than semantics.

A history lesson

The department's existence might be considered a miracle in itself. To Mr. Bennet's knowledge, no other medical institution in the world has its own department of people who collaborate to build things solely to improve patient care.

"It's probably an historical anomaly," he says. "The clinic was out here in the middle of nowhere, and people had to rely



Kevin Bennet (far right) is proud of his geek status, as are the other 53 members of the Mayo Clinic Division of Engineering and Technical Services. Front to back, right to left: Kevin Bennet, James H. Christensen, Steven Deick, April Horne, Raymond Phelps, Heidi Ellringer, Jonathon Lange, Bev Kundert, Alex Streeter.

on themselves to get the job done. From the very beginnings of the clinic, doctors performing surgery had to find a way to keep the surgical instruments in good shape. When something broke, it had to be fixed, and when something no longer worked, they had to create something that did. That mentality still prevails today: If it can be imagined, it can be built."

The records of an official engineering division at Mayo Clinic can be traced back to 1947, following the end of World War II. During the war, engineers at Waters Instruments, a private company in Rochester, were kept busy enough. But after the war, they found themselves without work. At that time, Mayo combined the skills of these engineers with the know-how of those working in the already-established instrument shop. Together, the two groups formed a department of people who could design and build almost anything.

When geeks and docs collaborate

"It's always been about more than just having a group of engineers who can envision and create gadgets," says Mr. Bennet. "As engineers, we succeed because nowhere

else in the world would we have immediate access to world-class researchers and doctors like we do at Mayo Clinic. If we need to get a better understanding of how something works or how a procedure will impact a patient long term, we just contact the doctors to get their insights. Being able to collaborate with everyone at Mayo is priceless. They're always willing to help, and we get the job done right because of that level of collaboration."

Mayo engineers design and build devices to the highest of standards.

"If Mayo finds one of our inventions useful, chances are the rest of the medical world will find it useful as well. If something we design turns out to be particularly helpful or in high demand, Mayo can then patent it and sell it commercially. Good ideas are good ideas and Mayo has always been about advancing medicine through the sharing of knowledge," Mr. Bennet says. ■

BEV KUNDERT Applying pressure to improve patient care

The need was simple. The solution seemed fairly obvious. Manufacturing the device was neither simple nor obvious, at least not at first blush.

The issue was pressure. Could surgeons and nursing staff apply uniform pressure to all points of a wound each time a dressing was removed and reapplied following a leg amputation? And was there a solution for the ongoing problem of having to remove the dressing multiple times a day to examine the surgical site?

The right answers

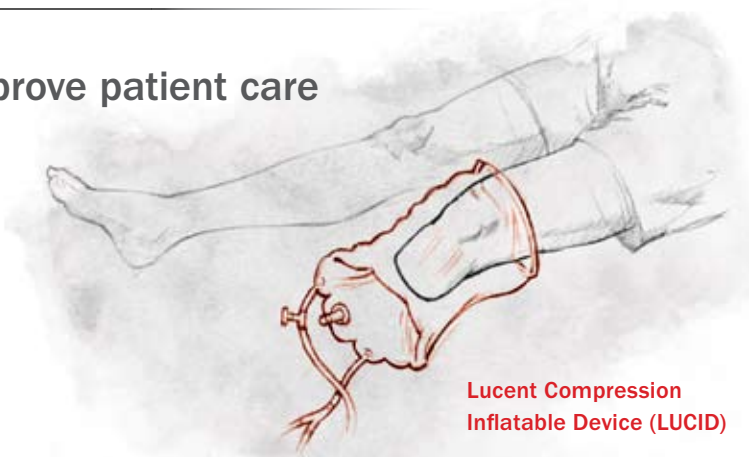
Thanks to the Division of Engineering at Mayo Clinic Rochester, the answer to both questions was “yes.” And these were the exact answers Thomas Shives, M.D., was looking for when he initially approached the division.

Dr. Shives, an orthopedic specialist at Mayo Clinic Rochester, and his staff faced a constant challenge in the 72 hours following a leg amputation. During this critical time, swelling must be controlled for the comfort of the patient and to aid in healing, both of which reduce hospital stays.



“It’s fulfilling when you see that the work you’re doing directly improves patient care. The LUCID device will help patients, and that’s a good feeling.”

— Bev Kundert



However, depending on who is wrapping the wound, the pressure on the leg could be more or less than the last time it was attended. To complicate this problem, each time the site needs to be checked for bleeding or signs of infection, the unwrapping and rewrapping cycle starts over.

Winning combination

But a combination of engineers and technicians — along with a breathable plastic and a transparent material — came together to create a device that fits the bill. From that mix, Lucent Compression Inflatable Device (LUCID) was born.

LUCID looks somewhat like a very small, transparent garment bag. However, inside the see-through exterior lies its genius: a breathable plastic to aid healing and a small tube connected to an automated pump that inflates to exact specifications and pressure each time it’s inflated. Pressure problem solved for Dr. Shives and his team.

Bev Kundert, electronics technician, was instrumental in creating the handheld device that gives LUCID its inflating power. After Chris Kimble, electrical engineer, led the design of the circuit board of the handheld gadget, Ms. Kundert put it together. “The goal was to make it as easy to use as possible,” says Ms. Kundert. “The keypad of the device has simple up and down arrows to control the amount of pressure. And the inflatable bag, which is placed over the dressing, has a zipper on the side and an air plug to quickly remove the bag, if needed.”

Another member of this winning team, Joel Kuhlmann, worked on the mechanical engineering end, designing the template for the transparent bag that fits over the amputated limb. “We had some problems getting the seams of the bag to weld together, but in the end, Tyler King, one of our mechanical welders, got it to hold,” says Mr. Kuhlmann. ■

ALEX STREETER “Chemistry set” helps with heart scans

Alex Streeter’s favorite project is something along the lines of an automated chemistry set, with a twist.

About a year ago, Mr. Streeter and some of his engineering colleagues got a mini-chemistry lesson from Mark S. Jacobson, the PET radiochemistry facility coordinator in Mayo’s nuclear medicine lab.

“Mr. Jacobson needed a machine to synthesize palmitic acid, a new radioactive chemical his lab wanted to use with positron emission tomography (PET) scans of the heart. But no commercially available device existed to synthesize this chemical, so we had to build it for them,” says Mr. Streeter.

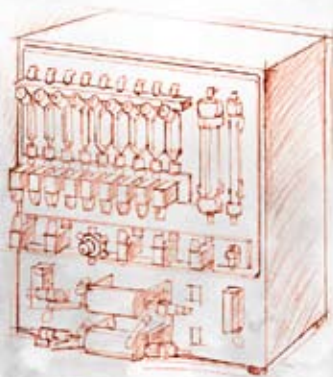
The lab uses radioactive chemicals, such as palmitic acid, for scans because these chemicals bind to specific tissues in the body, highlighting them for easier viewing. In this case, palmitic acid binds to specific heart cells, to evaluate cardiac metabolism — the rate of blood flow in and out of the heart.

“Mr. Jacobson found an article that described how to synthesize the chemical by hand. He needed a machine to synthesize this chemical, but learned that it didn’t exist,” says Mr. Streeter. “Synthesizing palmitic acid by hand isn’t an option since it’s radioactive and much too dangerous in the concentrations necessary. Plus, the chemical’s effects don’t last long, so it would have to be produced on demand for each patient, which would be time-consuming.”

Building it in reverse

Using reverse engineering, Mr. Streeter examined other machines in the lab that synthesize radioactive chemicals and designed custom parts to be made by the division’s machine shop and glassblower.

“It took quite a while to acquire the right parts, but during this design phase, I built the PET synthesis prototype on the computer by using a computer-aided design program that constructs 3-D models,” says Mr. Streeter.



Positron emission tomography (PET) synthesis module

“As far as we know, we are the only group in the world synthesizing palmitic acid for use in cardiac metabolism testing. This is cutting-edge medicine.”

— Alex Streeter



Testing, 1, 2, 3 (and 4, 5, 6)

“Every time we build something, it goes through a series of reviews,” says Mr. Streeter. “The project team looks at the design to analyze whether it will do the job intended. We have another group look at the device’s structure to see if it’s physically strong enough to support the load it’s going to be subjected to. Then it goes through the design-review process to make sure we didn’t miss anything. Then we showed it to Mr. Jacobson and his group. Although we understand how the device will be built, they better understand how it will be used.”

The PET synthesis module is now being built and will soon be put to the test synthesizing its radioactive load in a lead-lined enclosure. All the steps preceeding its construction were taken to increase the quality of heart scans at Mayo Clinic.

“Collaboration is the key,” says Mr. Streeter. “We had a proponent who needed the device built. We put it together, and we called in specialists from our mechanical team, our software specialists, our electronics group and our machinists to make it happen. As far as we know, we are the only group in the world synthesizing palmitic acid for use in cardiac metabolism testing. This is cutting-edge medicine.” ■

STEVEN DEICK Vial retrieval system helps search for samples

For almost a century, Mayo Clinic researchers have been collecting clinical samples — tissue, blood, blood components and bone — in an effort to one day find cures for the plethora of diseases studied here.

Today, with the explosion in genomics research, even more samples are being collected to help unravel the mysteries of life. This wealth of patient data is one of Mayo's greatest strengths.

Managing it is one of Mayo's greatest challenges.

Although this vast archive of samples places Mayo at the head of the pack in the genomics race, it also presents an enormous organizational problem. How do researchers find the samples they're looking for after they've been collected and stored?

Engineers to the rescue

Enter the Division of Engineering and Technical Services at Mayo Clinic Rochester.

The complexities of this retrieval nightmare came to light when orthopedic researcher, Mark Bolander, M.D., presented the cumbersome problem to the division. Steven

Deick, project manager, and his team of engineering gurus listened and then set about finding a solution. They studied the lab environment in detail for many weeks and discussed with lab technicians the existing method of organizing the vials in order to develop a solution. From these discussions, Mr. Deick and his team designed the Vial Archiving and Tracking System (VATS). In something resembling a modified claw machine at a penny arcade, VATS quickly and efficiently helps researchers locate and retrieve their prize — the needed vials — among thousands of similar samples.

The ins and outs

The whole VATS unit is about the size of a microwave oven and sits next to a standard-sized freezer in the research lab. As the lab technician identifies the next round of vials needed for study, VATS goes to work deciphering where those vials are located in the freezer. Knowing the exact location is a handy bit of knowledge for the technician who must open the freezer, which can be kept at temperatures as low as minus 320 degrees Fahrenheit.

Once retrieved, a square plastic box containing the vials is scanned by VATS and "checked out" by the technician. When the technician is done, the vials are placed back into any box in the freezer. VATS scans the box of vials a second time and updates the computer database with the vials' new location. Returning the vials anywhere in the freezer saves the technician time, and VATS ensures that technicians can always find the vials they need.



Grocery store technology

Vials are identified when a digital camera feeds the image of the contents of the box to a computer, which then analyzes the image and decodes each vial's two-dimensional data matrix code (think of a grocery store scanner identifying 81 bar codes simultaneously).

"Each two-dimensional code actually contains more information than needed, so even if a code is partially covered or is somehow damaged, the software will still identify the vial," says Mr. Deick. "The identification code may also be placed on the side of the vial as a safety measure. In addition to finding the vials needed, VATS will also let you know if a vial is misplaced."

The word is out

"The first unit was really built to solve a single-lab problem, but now it's catching on," he says. "We've had additional requests for VATS in other labs at Mayo and could realistically see 200 VATS units installed across all three Mayo sites. There is also the potential for commercially marketing this system."

"VATS is an excellent example of what we do in the Division of Engineering," says Mr. Deick. "Researchers and doctors come to us with a problem, and we go to work trying to design a solution to meet a need. VATS is an exceptional tool that advances Mayo's research efforts." ■

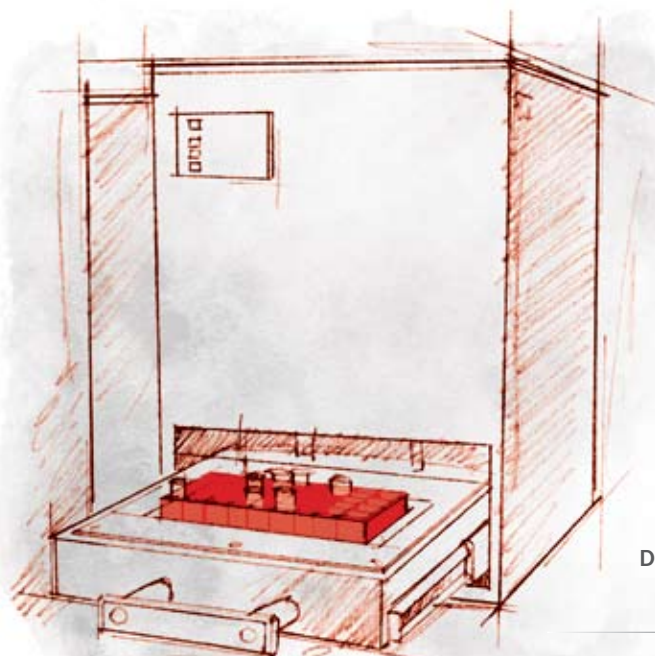


Steven Deick

The Vial Archiving and Tracking System (VATS) (D) quickly and efficiently helps researchers locate and retrieve needed vials (B) from among thousands of similar samples. VATS uses a two-dimensional data matrix code (C) to decipher where specific vials are located in a freezer. Once retrieved, a square plastic box (A) containing the vials is scanned by VATS and "checked out" by the technician. VATS ensures technicians can always find the vials they need.



C



D

By Matt Derechin

A WORLD of possibilities

Discovery of a mutation opens the door to dementia research

Maybe we'll find it today; maybe we'll find it tomorrow; or maybe we'll never find it. Those thoughts were all at the back of Jennifer Gass' mind when she started her day on April 7, 2006. A research technician at Mayo Clinic Jacksonville, she was in the midst of an exciting project: the search to find the gene responsible for an inherited form of frontotemporal dementia (FTD), which researchers had observed in several North American and European families.

She knew that discovering the gene would be an extraordinary find, one that would be relevant to the many patients around the world with FTD. For that reason, teams in several countries were racing to make the discovery.

But the search had become the proverbial needle in a haystack. Ms. Gass works in the research lab of Michael Hutton, Ph.D., and she had been looking for the gene for more than a year. Her work focused on studying 160 genes located on chromosome 17. And she was a relative newcomer to the project. Matt Baker, a senior research technologist in Dr. Hutton's lab; Bradley Boeve, M.D., a neurologist at Mayo Clinic Rochester; and Dr. Hutton had been searching for 10 years.

For this group, and for Rosa Rademakers, Ph.D., a visiting scientist who joined Dr. Hutton's lab in early 2006, the line between success and continued frustration turned out to be thin and red. A line with those features drew Ms. Gass' attention as she scanned the results of a DNA-sequence test for a little-known gene that produces progranulin, a protein that has previously been studied only by cancer researchers.

The sequence test analyzed DNA samples from seven patients with FTD and compared the results to samples from a small group of people without the dementia. The test generated a report that graphed each DNA sample, using colored lines that formed peaks corresponding to each person's DNA. And in one of the patient samples, two peaks overlapped: a blue peak, which was consistent with the reports for healthy people, and a smaller red peak, which was not consistent.

It was something that Ms. Gass had never seen before, but it was not, at first glance, proof of a mutation or disease causation. More tests would have to be done to prove if either of those possibilities was true.

A knockout gene

Over the next few days Dr. Hutton's team would discover that the patient samples had a mutated progranulin gene, a shortened version of the gene, missing about four pair of nucleotides — the individual components of DNA, which strand together in pairs. Checking other patient samples, the team soon found similar mutations at various points along the gene's code. No such changes were observed in samples from healthy people.

Further testing revealed that the mutations affected the gene's functioning. Ultimately, the team identified 23 different mutations in progranulin, and each one had the same effect. The mutations effectively knocked out one copy

What is frontotemporal dementia? FTD, the most common form of dementia after Alzheimer's disease and Lewy body disease, is a group of brain disorders that affect the frontal and temporal lobes of the brain, which control personality and language. It resembles Alzheimer's disease in many ways but usually affects personality and/or language first and affects memory functioning during later stages.



Left to right: Ashley Cannon, Jen Adamson, Jennifer Gass, Matt Baker, Rosa Rademakers, Ph.D., and in the foreground Michael Hutton, Ph.D.

of the gene. As a rule, people have two copies of each gene, which they inherit from their parents, so the mutations caused a 50 percent drop in the production of progranulin.

The team shared the news with a collaborator in Belgium, Christine Van Broeckhoven, Ph.D., and she discovered similar results in patient samples that she had. It was time to celebrate, says Mr. Baker.

“Discovering that the mutation was in another family and was linked to the disease was the final thing,” Mr. Baker says.

Meanwhile, in Manchester ...

An ocean away, Stuart Pickering-Brown, Ph.D., also had reason to celebrate. An associate professor at the University of Manchester, in the United Kingdom, Dr. Pickering-Brown spent two years in Dr. Hutton’s lab searching for the gene that Ms. Gass eventually found. Though he didn’t discover the gene, he helped lay the groundwork for its discovery, thanks to help from a Mayo benefactor.

Funds from a fellowship program established by Robert and Clarice Smith allowed Dr. Pickering-Brown to identify a large family in British Columbia with an extensive history of FTD. Analyzing DNA from this family, Dr. Pickering-Brown established two pieces of information that helped make the progranulin discovery possible.

First, he showed that the family members didn’t have any mutations in the tau gene, which previous research had

identified as a cause of FTD. That helped other scientists embrace the idea that there could be more than one genetic cause for the disorder.

Secondly, Dr. Pickering-Brown’s research helped narrow the search for the gene later discovered by Ms. Gass. Through various screening techniques, genetics researchers can compare DNA between family members who have a disease and those who are unaffected, to establish a general location for a disease-causing mutation. Dr. Pickering-Brown’s data yielded the 160-gene area that contained progranulin.

“I don’t think we would have found the progranulin mutations without the Smith Fellowship and the samples from this Canadian family,” says Dr. Pickering-Brown, who is listed as a joint first author on the paper in *Nature* that announced the progranulin discovery.

Indeed, the progranulin experience is a textbook example of why philanthropy is necessary for medical research, says Dr. Boeve.

“To find answers, we need to look down a bunch of avenues, and maybe only one in 10 of those avenues will turn up something; that’s just how medical research works,” he says. “But we have fantastic investigators and scientists and the infrastructure in the Birdsall Building (in Jacksonville) is fabulous. What it comes down to is funding, and to do this type of high-risk, high-reward work, we need philanthropy.”



Bradley Boeve, M.D.

A promising enigma

The progranulin finding is only an end to a beginning, and a surprising one at that. Prior to the discovery, no one had been studying progranulin's role in brain functioning. And the mutation's effects — a reduction in protein production — are also unusual because usually these changes cause genes to take on extra functions, not limit them, says Dr. Rademakers, who has published research showing that 5 percent of FTD patients worldwide have progranulin mutations.

But the mutation's effect may turn out to be an advantage from a treatment perspective, says Dr. Boeve, because it suggests therapy may not be far away. It may be possible to treat people who have progranulin mutations by using drugs that stimulate the production of progranulin, he says, and several drugs may be able to do that.

"We don't know why loss of progranulin causes people to develop a neurological disorder with symptoms that become evident between the ages of 50 and 70," Dr. Boeve says. "But at the same time, we may have an easier time developing therapies for FTD associated with progranulin mutations, in comparison to diseases like Alzheimer's or Parkinson's, which we know much more about."

Still, even this possibility only begins to describe the potential that studies of progranulin may have for FTD and other neurological disorders. Although the mutation is present in a relatively small number of patients, it leads to a brain pathology that is commonly seen in people with FTD. People with the mutations, and about 50 percent of all patients with FTD, have abnormal clumps of a protein called TDP-43 in their brains. These protein clumps are linked to the cell dysfunction and cell death that occurs in FTD.

"Not only do we now understand the cause of FTD in the rare individuals that have the mutations," says Dr. Hutton, "we now know one process by which this disease is caused in a large group of FTD patients."

Priming the progranulin pump

And there's more. The same protein, TDP-43, that clumps in the brains of people with FTD also clumps in the brains of people with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, but in a different part of the brain. Perhaps loss of progranulin has something to do with ALS as well. And Dr. Hutton says there's also evidence suggesting that progranulin may be relevant to Alzheimer's studies.

"We don't have the resources to investigate all of these possibilities," he says. "But these findings point to a fundamental question: What is progranulin's function in normal brain cell activity? We have to find out. The idea is to translate our genetic studies in order to mimic this form of FTD in animals and then to use that information to identify safe, effective therapies for patients."

Dr. Hutton is quite familiar with the path he describes. He and colleagues in the Neurosciences Department have used a similar blueprint to identify new treatments for other forms of FTD, as well as new possibilities for treating Alzheimer's disease. The Alzheimer's drug, identified by Todd Golde, M.D., is now in Phase II clinical trials, and FTD therapies are only a few years from the first phase of clinical tests.

In addition to working on therapeutics, Dr. Hutton and colleagues are already searching for another important gene related to FTD. Working again with patients and families from across the globe, they have traced their genetic suspect to a region on chromosome 9. It's particularly important because the mutation causes patients to develop both FTD and ALS, and it leads to the same pathology seen in FTD patients with progranulin mutations.

"When that gene is discovered, we'll have a huge part of the puzzle," Dr. Hutton says. "We'll have two genetic causes for that type of FTD, and we'll know the protein that accumulates in the brain. I know that gene will be found within the next year. Maybe not by us, but I know somebody is going to find it." ■

For information about dementia, please visit
www.mayoclinic.org/mayo-magazine.

The thrill of discovery



Jennifer Gass and Matt Baker

She doesn't call herself an explorer, a pioneer or any other grandiose term, but Jennifer Gass has witnessed some amazing phenomena, all the same.

A research technician in the lab of Michael Hutton, Ph.D., at Mayo Clinic Jacksonville, Ms. Gass made a discovery that most people in her field will never make. She identified a disease-causing genetic mutation for frontotemporal dementia (FTD), the most common form of dementia after Alzheimer's disease and Lewy body disease. These types of genes — and their discovery — are universally rare.

But, reflecting on the discovery, Ms. Gass says its rarity was only one of her initial thoughts. "For the first few minutes, my lab partners and I were the only ones in the world who knew that this gene was a cause of FTD," she says.

A great start

And it was a precursor of things to come, because in the next few weeks, Ms. Gass and her colleagues would find several more mutations in the same gene, called progranulin, that caused FTD. "We were finding about three mutations a day," she says. "It was the best feeling ever. It's why I chose a career in science."

As rare as the achievement was, she had someone who could relate to it: Matt Baker, a senior research technologist also in Dr. Hutton's lab. Mr. Baker experienced the same joy eight years earlier. In 1998, he found the first genetic cause for FTD, a mutation in a gene that produces a protein called tau.

"I was more excited this time around, perhaps even more so than Jennifer, who initially made the discovery, because of the effect the first discovery had on the group," Mr. Baker says. "It had an incredible impact on research in our field, and it generated grant funding for our lab. I know this latest discovery will have a similar effect."

The secret to success

Mr. Baker says Mayo's strong clinical practice is the key because it attracts large numbers of research participants, which is vital for any genetics research. But Dr. Hutton says the technologists are an important piece of the puzzle.

"It's a testament to their skill," says Dr. Hutton. "It's very easy to miss small changes when you're looking at gene sequences day after day. Even though they'd seen so many DNA sequences, they didn't miss the one that counted."

The lab environment is also an important factor, Mr. Baker says, because Dr. Hutton expects research technologists to contribute to each project. The importance of these contributions are evident in the publications that result from the research, which frequently include Mr. Baker, Ms. Gass and their colleagues as co-authors. Indeed, Mr. Baker has established an impressive curriculum vitae during his 10 years with Dr. Hutton.

"Quite a few senior scientists in the field have commented that Matt's CV is comparable to the average professor," Dr. Hutton says.

That's another interesting aspect to this story. In Mr. Baker's case, the discoveries over the years have never given him the urge to pursue a doctoral degree. If anything, he is more comfortable in his career choice. "I love my job," he says. "It doesn't make sense for me to pursue a Ph.D.; it would change things too much."

But Ms. Gass is already pursuing a master's degree and the progranulin discovery has her thinking seriously about pursuing a doctorate. "It's a huge decision, but this experience has truly opened my eyes," she says. ■

By Dianne M. Axen

The EXTREME makeover of viruses

Using the measles virus to treat ovarian cancer

The idea of using a virus to fight cancer is not new. Animal studies using viruses date back to the 1940s, but the technology and the basic facilities and equipment necessary to manufacture a gene or virus therapy pure enough to meet the Food and Drug Administration's (FDA) standards for use in humans has always been the challenge.

In 1998, Mayo Clinic made a commitment to advance its program of gene and virus therapy by recruiting hematologist and scientist Stephen Russell, M.D., Ph.D., from Cambridge University in England to direct Mayo's Molecular Medicine Program.

"I've had a passion my entire career for harnessing the destructive power of viruses and using them to destroy tumors," Dr. Russell says. "Coming to Mayo was the opportunity of the century for conducting the translational research that will help us achieve that goal."

In only eight years, the Molecular Medicine Program at Mayo has grown in expertise and infrastructure to become one of the very few places where clinical-grade reengineered viruses and viral vectors can be manufactured all the way through to patient use.

Oncolytic viruses are cancer-killing viruses. ("Onco" means cancer, "lytic" means killing.) They represent a potential new cancer therapy called virotherapy — which uses the natural properties of viruses to kill cancer cells.

"Moving this work from lab to clinic absolutely requires teamwork, and I think that is one of the reasons we can successfully do this at Mayo and why other centers have such a huge problem getting this to work," Dr. Russell says. "Teamwork is part of the culture here, and it's very easy to spark direct collaborations that enable bench-to-bedside translations to occur."

The team includes scientists who engineer and test the new therapeutic agents. It also includes a Toxicology Core where the pharmacology and potential toxicity of these new drugs are evaluated prior to human use, a Viral Vector Production Laboratory where clinical-grade viruses are manufactured for human use, and clinicians who design and execute the clinical trial protocols. In addition, there are nurses and study coordinators who look after the clinical trial patients and the clinical trial analysis laboratory, which performs the necessary correlative studies on samples obtained from patients participating in the clinical studies.

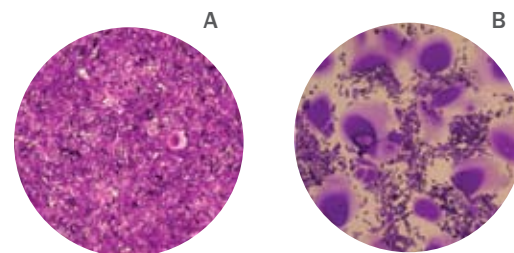
Reengineering viruses to kill cancer

The key to successful gene therapy is the vectors, says Dr. Russell. A vector is a vehicle that carries a gene into a cell. Viruses are nature's vectors for delivering genes into cells.

Viruses, such as measles, are natural vectors and are very clever about how they get inside a cell. Most viruses contain one or more genes that direct the activity of the virus. The idea behind virus therapy is to remove the original "harmful" gene — such as measles, and replace it with a different gene — one that carries a "helpful" message.

The reengineered virus becomes an efficient delivery device. Like a tiny missile, the virus is programmed to target specific cells such as cancer cells. Once inside the cancer

Human cancer cells before (A), and after (B) infection by the reengineered measles virus. Infected cells fuse together to form large, single masses, which eventually die as a result of the self-destruct message they receive from the measles virus. Healthy cells are left alone.



Stephen Russell, M.D., Ph.D.

"I've had a passion my entire career for harnessing the destructive power of viruses and using them to destroy tumors."

— **Stephen Russell, M.D., Ph.D.**

cell, the virus delivers its payload — a suicide message that instructs the cancer cell to self-destruct. Only cancer cells are targeted, healthy cells are left alone. This major cancer-fighting advantage has the potential to eliminate many of chemotherapy's uncomfortable and toxic side effects.

Restructuring the measles virus

In July 2004, the Molecular Medicine Program at Mayo Clinic launched the first gene therapy clinical trial that included the entire preclinical cycle. Kah Whye Peng, Ph.D., one of the project's lead investigators, engineered a measles virus, MV-CEA. The next phase was to manufacture the vector and study the effects of the treatment. In a May 2002 paper in *Nature Medicine*, Drs. Peng, Russell and their colleagues described a technique that created the ability to monitor gene expression with a simple blood test.

"One of the shortcomings of past gene therapy clinical trials was the inability to understand why it fails — was it failure of gene delivery, or did it just not work?" says Dr. Russell. "You cannot improve the biotechnology if you do not know what part went wrong." Researchers had an important new tool to take their research to the next level.

When studies showed that MV-CEA induced regression of 80 percent of ovarian tumors in mice, the team was ready to launch a clinical trial. The clinical trial was the first step in studying its effect for women who have progressive ovarian cancer that has not responded to standard treatment.

"Recurrent ovarian cancer is a lethal disease, claiming the lives of 14,000 women every year in the United States. It's exciting for our team to take this virotherapy approach all the way from discovery to a stage where it can help our patients," says Eva Galanis, M.D., the study's principal investigator.



Dixie Manley

Beginning human studies

Dixie Manley, 67, of Cedar Falls, Iowa, was the first human to receive the reengineered measles virus anywhere for any reason. In July 2004, she participated in the Phase I clinical trial at Mayo Clinic Rochester.

"Being the first patient to take the plunge in the early phase of clinical research is really a very brave thing to do," Dr. Russell says. "It is completely new territory."

Ms. Manley received the medication in the Clinical Research Unit, Mayo Clinic's facility designed specifically to conduct clinical research projects. "I was never worried about participating in the clinical trial, but when I had my first treatment, the room was full of people," Ms. Manley says.

The reengineered measles virus was diluted in a half liter of saline and the medication was administered through a catheter in the abdominal cavity, where it could come in direct contact with the tumor.

"I knew from the beginning that this research might help me a great deal, or it might not help at all, but I felt that if it didn't help me, it could possibly lead to something that might help other people."

— Dixie Manley

"I knew from the beginning that this research might help me a great deal, or it might not help at all, but I felt that if it didn't help me, it could possibly lead to something that might help other people," Ms. Manley says.

One of the study trial goals was to study the safety of dose amount and timing. Ms. Manley received six cycles of medication with very minimal side effects.

"It's very exciting for our team to take this virotherapy approach all the way from discovery to a stage where it can help our patients."

— Eva Galanis, M.D.



Eva Galanis, M.D.

“Although a Phase I clinical trial is too early in the research process to draw conclusions about the effectiveness of a treatment, there has been early evidence of biologic activity of MV-CEA in ovarian cancer patients,” Dr. Galanis says. “The excellent tolerance is also allowing us to test higher doses of MV-CEA in this ongoing trial.”

Developing drugs with a “patient first” commitment

Mayo Clinic’s commitment to patients ensures that the majority of gene and virus research at Mayo is motivated by a problem seen at the bedside. Ovarian cancer was first, but clinical research is under way at Mayo on several tumors including brain cancer and multiple myeloma.

Gene and viral therapy is being studied not only in cancer, but in many diseases. “It would be difficult for me to think of any disease for which there isn’t currently some form of gene therapy effort going on,” Dr. Russell says.

Molecular medicine is a whole new model for how drugs are designed, built and tested. It is much different from the discoveries of large drug manufacturing companies. Yet, anything being developed at Mayo will be transferred to industry at some point so that others can benefit from the treatment.

“The question of when to do that is a difficult one,” Dr. Russell says. “But on the other hand, the drug is never going anywhere unless we transfer, so it is a very important issue.”

In the case of MV-CEA, Mayo has recently licensed the measles technology to a pharmaceutical company. The company will be responsible for manufacturing the product and distributing it in large quantities to all medical centers who will participate in Phase II trials and beyond.

“Although it’s a complex process, it’s incredibly positive that we are at a point where transfer to industry is even possible,” says Dr. Russell. “There are very few centers in the country capable of doing this.” ■

Creating cures of the future



Mark J. Federspiel, Ph.D., and in background, Kirsten Langfield and Troy Wegman

There was great excitement at Mayo Clinic when the reengineered measles virus, MV-CEA, was launched. This was the first gene-therapy clinical trial in which the entire cycle, from basic research to testing in patients, was conducted on a Mayo campus. Worldwide there are very few institutions with this capability.

Mayo Clinic’s Viral Vector Production Facility, directed by Mark J. Federspiel, Ph.D., must uphold high standards of cleanliness and sterility to comply with Food and Drug Administration regulations as the facility goes through many rounds of harvesting, testing and purification of the viral products for human use.

“If we had to contract out the manufacturing to a biopharmaceutical company, we would be a long way from being able to provide this experimental therapy for patients,” says Dr. Federspiel. “Having the facility on campus means we can collaborate on solving problems as they arise.”

Dr. Federspiel and his team are already translating the knowledge derived from manufacturing MV-CEA into subsequent projects, manufacturing other viral products and making it possible to produce purer products with greater efficiency. ■

VVP team members include: Guy Griesmann, Linda Gregory, Kirsten Langfield, Julie Sauer, Sharon Stephan, Henry Walker, Troy Wegman, Cindy Whitcomb

By Dianne M. Axen

Barbara Koenig, Ph.D.

Co-director of the Program in Professionalism and Bioethics

The biomedical revolution holds the promise of tailoring medical treatments and prevention strategies to each person's unique genetic makeup. This level of scientific discovery brings excitement and enthusiasm, and yet, every scientific advance potentially has unanticipated consequences as well as benefits. Barbara Koenig, Ph.D., recognized this early in her clinical career and has spent more than 20 years researching how medical advances and discoveries affect people and health policy.

Dr. Koenig has been actively involved in research on end-of-life issues and the ethical, legal and social implications of the genomic sciences. Born in St. Paul, Minn., she is a University of Minnesota graduate in history and nursing. Dr. Koenig received a Ph.D. in medical anthropology from the University of California, Berkeley and San Francisco. She joined the Mayo Clinic staff in the summer of 2005, moving from the Center for Biomedical Ethics at Stanford University, where she was executive director for 10 years.

Dr. Koenig has a national presence in the area of ethics in contemporary medicine. She is a member of the Ethics Advisory Committee for the Centers for Disease Control and Prevention with the task of identifying public health issues related to the study of genomics. Dr. Koenig has authored numerous scientific papers and book chapters. Her newest book is *Revisiting Race in a Genomic Age*. As professor of medicine at Mayo Clinic and as faculty associate for the Center for Bioethics at the University of Minnesota, Dr. Koenig plans to build an active, interdisciplinary bioethics program with collaborative links between the two institutions. She discusses her research interests and thoughts on medical ethics with Mayo Magazine.

What does bioethics mean to medical practice at Mayo Clinic?

Trying to figure out how to balance harms and benefits is not an easy task. Bioethics means applying ethics to the fields of medicine and biomedical science.

There's a tendency to believe that every good doctor is ethical. But what does that really mean? You might think it's simply someone who follows a set of rules. Another way of thinking about ethics is to link it with notions of virtue. In a line of thinking going back to Aristotle, ethics is never as easy as simply applying a set of rules; it requires complicated judgments by skilled practitioners. This view of ethics fits well with Mayo's strong culture of professionalism.

Sometimes bioethics means asking the hard questions. It's not an easy role. There are times when I have to voice the things that people might not want to talk about, so it can be a little uncomfortable. In my role at Mayo Clinic, I consider myself a catalyst working with clinicians, scientists and researchers who are grappling with the complex ethical questions that are central to practice.

How does scientific discovery bring ethical challenges?

Scientific discovery brings ethical challenges because it's a social process — it's not simply a technical process. And it's through a very complicated process that we come to understand that we have a moral obligation to apply a particular discovery. How do we get it right?

The thing about technologies is they don't stay in their neat little boxes. Let's say we develop technology to test for cancer susceptibility. It seems like a good thing; it can be used to recommend screening tests for certain people who may be at risk. But we then face figuring out how to help people live their lives "at risk" for illness that may or may



Barbara Koenig, Ph.D.

not develop. It also means that it's immediately possible to translate a test to other arenas. At what point do you draw the line in using it? For example, should it be done in prenatal genetic testing, given that most cancers don't develop until later in life? These issues quickly become complicated and controversial.

Is it ever possible to address ethical challenges before they occur?

By thinking about the ethical issues up front, I definitely think it's possible to minimize some, but not all, of the unwanted consequences of innovation and discovery. In fact, I sometimes describe my career as doing proactive bioethics in public. For example, one of my current projects relates to the genetics of addiction. With funding from the National Institute on Drug Abuse, our group is trying to think through the implications of scientific discoveries that draw links between genetics and addictive behavior. We ask questions such as: How will a novel scientific understanding of addiction affect health policy? What are the implications of identifying individuals as having a genetic susceptibility to alcoholism or to behaviors like smoking? Questions like these are at the core of our research. We work closely

with scientists and clinicians in the Mayo Clinic Samuel C. Johnson Genomics of Addiction Program. The goal of the bioethics research program at Mayo Clinic is to address challenges early in the research process.

How is bioethics involved in research such as individualized medicine at Mayo Clinic?

Individualized medicine means that new approaches to disease prevention and treatment will be developed based on an individual's unique genetic makeup.

One concrete example of bioethics research in the area of individualized medicine is a research project we are doing about collecting and storing DNA samples.

The future of individualized medicine hinges on the availability of high-quality DNA. In order to be useful clinically, DNA samples must be collected and linked to a particular individual so that the medical records, health outcomes and other information can be followed over time. This will involve volunteers who are willing to bank samples of their DNA in a context of trust. The question is: What is the best way to ensure that trust?



“Scientific discovery brings ethical challenges because it’s a social process — it’s not simply a technical process.”

— **Barbara Koenig, Ph.D.**

How do you respond to that challenge?

One of the first things our research project is doing is conducting a formal community consultation with residents of Olmsted County, Minn. In that community consultation we are helping research participants to understand the basics of banking their DNA. The next step is collecting detailed information from the group about their thinking on this issue. We are trying to learn what moral and practical concerns people have about contributing their DNA to Mayo Clinic research. The promise of individualized medicine will not be met without the ability to link DNA specimens to a person’s health records. However, we must first develop a way to ensure public participation in social decisions about banking DNA.

What influenced your decision to join the staff at Mayo Clinic?

One of the reasons I came to Mayo is that I believe it’s a unique institution that has long-standing traditions around certain problems that are of particular interest to me.

Can you give us an example?

One of the most serious problems facing health care today is the whole arena of end-of-life issues. This is one area where I’m trying to be a catalyst by convening what I’m calling an end-of-life stakeholders’ group. My role is in getting various Mayo staff together who hadn’t thought of themselves as having shared interests and helping them to develop innovative research. We are trying to learn what works at Mayo, what doesn’t and what unique projects we could do here.

What do you see as some of the unique strengths of Mayo Clinic?

Mayo’s structure is different — from its group practice model, not-for-profit status, salaried physicians, to its strong rules and regulations governing conflict-of-interest issues. To continue to place the best interests of the patient first, we face many challenges and must continue asking questions.

Because of Mayo Clinic’s unique structure, I think we can do certain types of innovation here that couldn’t be done elsewhere. I think if Mayo can solve some of these challenging problems, we might serve as a national model.

As a researcher, I am very interested in the kind of trust that Mayo patients have in their physicians. This is an incredibly valuable asset in working out the details of individualized medicine or improving care for patients facing the end of life. But trust is an asset that could be jeopardized by changes in health care. My role at Mayo allows me to think broadly about some of the central issues facing Mayo. It’s a luxury and a privilege to be able to do that. ■

By Michelle Felten

Waldenström's Macroglobulinemia

"SMALL" DISEASE with big consequences

David Lively and Richard Weiland aren't blood relatives. But they are "related" by blood in a different sense. Both men have Waldenström's macroglobulinemia (WM), an extremely rare blood cancer in which abnormal plasma cells multiply out of control, invading bone marrow, lymph nodes and the spleen.

And although they aren't kin, Mr. Lively and Mr. Weiland are two members of a very small family — those who have this cancer. In fact, the WM family consists of only about 10,000 of the 300 million people in the United States. The stats for worldwide WM prevalence aren't much higher.

Their stories

Currently the prognosis for those with Waldenström's is as small as the number of people who have it. The average life expectancy following diagnosis is five to seven years, although this prediction is changing for the better. Mr. Lively is a testimony to this. His diagnosis came in 1987 after he sought medical care for vision loss, ongoing back pain, fatigue and weight loss. "I was very lucky to find Dr. Robert Kyle at Mayo Clinic, one of very few experts on WM and a personal friend of Dr. Waldenström's. I went to Dr. Kyle for a second opinion," says Mr. Lively.

"In a sense, it was almost like winning the lottery, although it wasn't the kind of lottery anyone would want to win. Waldenström's is a very, very rare cancer, and then I was one of a tiny fraction of people who got the disease before age 40. Most people with WM are diagnosed at age 65 and older," says Mr. Lively.

Mr. Weiland's diagnostic scenario more closely matches the norm. He was diagnosed just three years ago at age 68. "I was diagnosed on Oct. 13, my birthday," he says. "I had been

seeking care for what I thought was an ongoing bronchial condition. I'd lost 30 pounds, I was having trouble with my eyesight, I was exhausted, and one morning as I was running up the stairs at my home, I fainted. That's when I knew something was really wrong. As I look back, I now realize I probably had Waldenström's a good two to three years before it was diagnosed, but the symptoms I was experiencing just seemed to be the result of aging. It didn't occur to me that it was anything more than just getting older and slowing down.

"Of course as soon as I was diagnosed, my two daughters, who both live in Rochester, started sending me information from Mayo Clinic. It wasn't long before I came here for treatment and help. I feel blessed to be so close to Mayo and so close to quality medical care," says Mr. Weiland, who lives in Northfield, Minn., about 50 miles from Mayo Clinic Rochester.

Fighting for their lives

Although their diagnoses came 16 years apart and at a different point in each man's life, the two share similar stories of the barrage of treatments they've tried and the endless clinical trials they've enrolled in, all in an effort to find a cure for this incurable cancer.

Waldenström's macroglobulinemia was discovered in 1944 by Swedish physician Jan Gosta Waldenström. More than 60 years later, the disease remains so rare that most physicians have never even seen, let alone treated, anyone with WM. And the tendency is for doctors to treat WM with the same chemotherapy drugs used for multiple myeloma or chronic lymphocytic leukemia, both cancers of the immune system. Historically, this one-size-fits-all treatment approach has proven ineffective for suppressing WM.



Richard Weiland and David Lively

"Ten years from now, we hope that Waldenström's will become a chronic condition instead of a death sentence."

— David Lively

Lights at the end of the tunnel

For Mr. Lively and Mr. Weiland, the rays of hope at the end of the long WM tunnel come in two forms: a foundation established solely to provide accurate information and a source of strength for WM survivors; and fundraising efforts that have netted more than \$2 million for WM research.

Foundation support for WM survivors is extensive, considering the rarity of the disease. The International Waldenström's Macroglobulinemia Foundation is 2,500 members strong and growing. The foundation, established in 1994, was developed and is financed solely by patients and their families. The foundation serves as an invaluable resource for those searching for what little information exists on WM. It also offers an impressive assortment of education materials, information about the more than 50 support groups across the country, a telephone lifeline, a quarterly newsletter and a Web site (www.iwmf.com) packed with information about the disease. There's even a section on the site tailored for doctors who are looking for information on how to treat patients with Waldenström's. Among the information found in this section is the book, *WM, a Review of Therapy*, by Morie Gertz, M.D., a hematologist at Mayo Clinic Rochester and an international expert on Waldenström's.

As for the foundation's fundraising efforts, the phrase "small, but mighty," seems appropriate. Just over a decade old, this foundation, made up of volunteers, has raised an impressive amount of money for WM research. The fund-

raising efforts have been as grassroots as the foundation itself with members holding benefits, selling raffle tickets, sponsoring golf outings, participating in fishing contests and even rowing a boat down the panhandle of Florida, gaining pledges for miles rowed. These personal efforts speak volumes about the members' commitment to their cause.

A little success goes a long way

"What's driving us now is the success we've seen with WM research in the past 10 years," says Mr. Lively. "For example, 10 years ago, rituximab was approved by the Food and Drug Administration for other forms of lymphomas. Although it's still not specifically approved for WM, studies show that about 50 percent of people with Waldenström's are able to put their disease into some level of remission by taking this drug. That's an incredible step for us. And the recent successes in genetic and cellular WM research create the need for more research. Our recent progress is good when you consider that there are only about 50 researchers in the entire nation working on WM, and about 20 of these researchers are at Mayo Clinic."

"Years ago when you were given a diagnosis of Waldenström's, it was sayonara and goodbye, get your affairs in order. But just look at the progress we've made in the past decade. Ten years from now, we hope that Waldenström's will become a chronic condition instead of a death sentence," says Mr. Lively.

He and 10,000 of his family members share that hope. ■

Financing a cure for Waldenström's

Waldenström's macroglobulinemia is an extremely rare blood cancer affecting only about 10,000 of the 300 million people in the United States. The disease is characterized by abnormal plasma cells multiplying out of control in the bone marrow, lymph nodes and the spleen.

Unfortunately for those who have Waldenström's, the rarity of this cancer puts it fairly low on the research agenda, behind more prominent cancers such as breast and colon, which affect millions of people each year.

Still, the rarity of the disease attracts researchers like Stephen Ansell, M.D., Ph.D., a hematologist at Mayo Clinic Rochester. His curiosity about what makes Waldenström's tick, or rather grow, recently garnered him a \$516,000 grant from the International Waldenström's Macroglobulinemia Foundation (IWMF).

The grant will be used over a three-year period to study molecules such as B-lymphocyte stimulator (BLyS) that control the growth and survival of malignant B-cells.

In people with Waldenström's, BLyS also stimulates immunoglobulin (IgM) overproduction. IgM is the portion of the blood that contains antibodies. B-cells are a type of white blood cell needed to fight infection.

"My specific interest in Waldenström's macroglobulinemia is in trying to understand how BLyS contributes to the growth and survival of malignant cells and why it leads to the overproduction of IgM," says Dr. Ansell. "If we could figure out how to switch off the increase in malignant cells and the overproduction of immunoglobulin, perhaps we could eliminate the side effects often seen with Waldenström's. It's these side effects (enlarged lymph nodes or spleen, extreme fatigue, headaches, weight loss, visual problems, tendency to bleed easily, confusion, dizziness and loss of coordination) that usually lead those with Waldenström's to seek treatment.

As part of this fight, Dr. Ansell and his research colleagues, Sherine Elsawa, Ph.D., and Anne Novak, Ph.D., have set a lofty goal for themselves: With the IWMF grant money, they'd like to identify cellular pathways that researchers can target in treating Waldenström's macroglobulinemia.

"Once we know what helps these malignant cells grow and survive," says Dr. Ansell, "our job is then to learn how to switch them off. If we can figure this out, this discovery



Stephen Ansell, M.D., Ph.D.

"My goal is to help patients with Waldenström's by finding a way to reduce the disease effects that make their lives miserable."

— Stephen Ansell, M.D., Ph.D.

will not only help those with Waldenström's, it might have a broader applicability to other cancers of the blood such as lymphomas and myelomas.

"We appreciate the grant money provided by the IWMF and look forward to giving the foundation a good report on our progress. This foundation is to be commended for the work it does in supporting Waldenström's research."

This is the second such grant Dr. Ansell and his colleagues have received from the IWMF. The first grant, more than \$400,000, was awarded two years ago. ■

Stewardship report

The many ways you can support Mayo's mission

The stewardship pages highlight members of our recognition groups. Many benefactors choose to belong to one or more of these groups to enhance their philanthropic experience.

Mayo Principal Benefactors

The designation of Principal Benefactor was established in 2003. It honors individuals and organizations who contribute \$1 million and more to support the mission of Mayo Clinic. We are honored to recognize an elite group that represents the foremost supporters of Mayo Clinic. By supporting innovation and discovery, these benefactors touch the lives of people throughout the United States and around the world.

Contact: James Hodge
hodge.james@mayo.edu

Mayo Major Benefactors

The designation of Major Benefactor was established in 1970. It honors individuals and organizations who contribute \$100,000 and more to support the mission of Mayo Clinic. These philanthropic gifts help Mayo Clinic provide the best care to every patient every day. They also support medical innovations that benefit people throughout the United States and around the world. The generosity of these gifts help Mayo uphold the tradition of its founders.

Contact: James Lyddy
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Mayo Annual Giving Program

The Mayo Annual Giving Program was established in 2000. It is Mayo Clinic's newest membership organization and is the only annual giving group of programs offered at Mayo Clinic. Annual contributions ensure that Mayo will have the necessary resources to continue providing compassionate

care for our patients, advancing medical progress and educating future physicians. Members of this group can provide annual support at one of six giving levels ranging from our Mayo Friends level of \$1,000 a year, to our Mayo Leadership Circle level of up to \$99,999 in a calendar year.

Contact: Jim Isaak
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The Mayo Legacy

The Mayo Legacy is an organization of Mayo patients, staff and benefactors who provide a bequest in their will or another type of planned gift to support our work. There are no membership fees or required gift amounts to join The Mayo Legacy. Currently, more than 3,200 individuals belong to The Mayo Legacy. Members live in 50 states and 14 countries.

Contact: Laird Yock
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The Doctors Mayo Society

The designation of The Doctors Mayo Society was established to honor individuals who provide alumni financial support for Mayo programs. Gifts are given to perpetuate the excellence of medical practice, education and research at Mayo Clinic. This benefactor category is open to members of the Mayo Clinic Alumni Association, Mayo Clinic Administrative Voting Staff and public members of the Mayo Clinic Board of Trustees.

Mayo Alumni Laureates

The designation of Mayo Alumni Laureates was established to honor benefactors who are alumni of Mayo Graduate School, Mayo School of Graduate Medical Education or Mayo Medical School, as well as their spouses.

Contact: Robert Giere
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For more information on philanthropy at Mayo, please visit: www.mayoclinic.org/development

PRINCIPAL BENEFACTORS: **Raymond and Roma Wittcoff**

Commitment to community

By Suzanne Winckler

When friends talk about Raymond and Roma Wittcoff, they invariably mention what unique individuals they are and what a remarkable couple they make.

Natives of St. Louis, Mo., the Wittcoffs began wintering in Arizona in the 1990s. They now reside there permanently, but they have not retired. The Wittcoffs have simply transported their passion for worthy causes to a new landscape. Their philanthropy, individually and as a couple, reflects their commitment to the elements that build strong communities — education, medicine, arts and environment.

Income, independence, influence

After returning from World War II, Mr. Wittcoff worked for his father's company in St. Louis — a manufacturer and distributor of men's hats.

The business had been very successful, but the younger Wittcoff predicted that the fashion was waning. With his father's encouragement, Raymond Wittcoff diversified, moving from hats to real estate and development. At one time he considered a life in academics, but he loved the action of the business world and knew that success in business would bring him the Three I's — income, independence and influence. He wasted no time.

Mr. Wittcoff was a pioneer in public television, helping to found KETV-Channel 9 in St. Louis and to develop the national educational television network, now known as the Public

Broadcasting System (PBS). He was also instrumental in the redevelopment of downtown St. Louis and the merger of Barnes and Jewish Hospitals.

Mrs. Wittcoff has amplified the spheres of her husband's interest, bringing to their bond a passion for music and the environment. She has served on the boards of the Saint Louis Symphony Orchestra, Opera Theatre of Saint Louis and Missouri Botanical Garden.

Together, the Wittcoffs are especially committed to education — both are trustees emeriti of Washington University, and she is a board member of the Technion-Israel Institute of Technology in Haifa. They're also committed to health care. Since moving to Arizona, they've focused much of their philanthropy on Mayo Clinic, supporting medical research, the Mayo Clinic Hospital, the Mayo Clinic Specialty Building and Mayo Clinic's Health Policy Center.

Wise counselors

The Wittcoffs serve on Mayo Clinic's Leadership Council in Arizona, one of a nationwide network of advisory boards that support the mission of Mayo Clinic.

They see an important role for Mayo Clinic in 21st-century medicine and patient care. And last May, Mr. Wittcoff participated in Mayo



Roma and Raymond Wittcoff

Clinic's National Symposium on Health Care Reform, where he joined more than 200 national leaders representing business, health care, government, public policy and patient advocacy.

The Wittcoffs consider Mayo Clinic a beacon of hope. "Mayo is a symbol of what this country is about," says Mr. Wittcoff. "And I think in proportion to the progress that is made by Mayo in medicine, it is contributing to those things that will win for us the affection and respect of the world." ■

PRINCIPAL BENEFACTORS: William and Sharon Schoen

Fostering leadership and integrity

By Patricia R. Martin

Military service and medical school may seem very different to many people, but not to William and Sharon Schoen. To the Schoens, both exemplify service to others, integrity and leadership. To reflect these values, the Schoens have established a scholarship at Mayo Medical School for honorably discharged members of the U.S. military.

Mr. Schoen, who dropped out of high school at age 15, later enlisted in the U.S. Marines. "The Marine Corps was the turning point in my life," he says. "At 19, I was a platoon sergeant, leading guys a lot older than me. I learned about real leadership."

These skills helped him earn an undergraduate degree and Master of Business Administration degree from the University of Southern California (USC) and contributed to his success in business. Mr. Schoen was president of a glass container company in Pennsylvania and then a brewing company in New York before taking early retirement in Florida. Retirement didn't last. Instead, over the next decade, he founded a bank and became president and CEO of a company that owns hospitals in small cities and rural areas.

Semiretired now, Mr. and Mrs. Schoen are turning their attention to a family foundation they created.

"Philanthropy is very rewarding for us," says Mrs. Schoen, who is president of the Schoen Family Foundation. Their four children also



Sharon and William Schoen

are involved in the foundation, which currently supports scholarships for military veterans at the USC business school, programs for adult learners and projects for the homeless, as well as Mayo Clinic.

The Schoens' association with Mayo dates back almost 20 years, when Mr. Schoen sought care for a persistent skin condition. A dermatologist at Mayo Clinic Jacksonville referred him to the Mayo Clinic Rochester surgeon who had developed a laser procedure to treat the condition. "We were very happy with the success of the treatment," Mr. Schoen says. "Mayo Clinic is an outstanding organization in every respect."

A few years later, W. Eugene Mayberry, M.D., who was CEO of Mayo Clinic in the late 1980s and who also serves on the board of Mr. Schoen's hospital company, referred him to

Robert Frye, M.D., for assessment of some heart issues. "Dr. Frye is another great Mayo doctor, and he leads a terrific team," Mr. Schoen says.

The Schoens think so highly of Mayo Clinic that they have created a distinctive scholarship program for medical students who have served two or more years of active duty in a branch of the U.S. military. "Our goal is simple: to assist vets who qualify for Mayo Medical School so that they can become physicians," Mrs. Schoen says.

Mr. Schoen notes that in all of his businesses, he has actively sought opportunities to hire military veterans. "They have demonstrated leadership and integrity, and these are qualities Mayo looks for in its students and physicians," he says. "We are happy to help veterans at Mayo Medical School." ■

MAJOR BENEFACTORS: **Bob and Laurie O'Gorman**

Building on the ironies of life

By Michelle Felten

Prior to 1960, Bob O'Gorman sold John Deere tractors and combines to farmers for use in their fields. After 1960, he sold the food that likely came from those fields at the local grocery store that he and wife, Laurie, owned.

There is a certain irony in selling farming products to farmers who grew the food that he would later sell. An even greater irony is that before he owned a grocery store, Mr. O'Gorman had never set foot in one.

"I didn't know anything about the grocery business," says Mr. O'Gorman. "But a friend of mine came to me one day and said that I ought to open a grocery store, the town needed one. We had several mom and pop stores, but people were going out of town to do their bigger grocery shopping and we had to figure out a way to keep them here."

"Here" is Cannon Falls, Minn.

Over the years, the O'Gormans owned several stores in southern Minnesota. "Every time I wanted to buy another store, I'd have to talk Laurie into it. She always thought we had enough stores. It got to be a joke after a while when people would ask, 'What's Laurie think about buying another store?' and I'd tell them she said no, and they'd say 'Well, then, it must be OK,'" says Mr. O'Gorman.

Ironically, it always was OK.



Bob and Laurie O'Gorman

"We worked really hard for many years," says Mrs. O'Gorman. "All seven of our kids worked right along beside us. I think that kind of family business teaches you about work ethic and about making good decisions. Working that closely kept our family strong."

The family drew upon that strong bond when oldest son, Dan, was killed in a car accident in 1975. "He survived four years in Vietnam only to come home and die in a car accident," says Mr. O'Gorman. "Now that's ironic."

But the O'Gormans know Dan's death helped bring them closer together and taught them to appreciate the things they'd sometimes taken for granted.

One thing the O'Gormans have never taken for granted, however, is the care they receive at Mayo Clinic.

Mr. O'Gorman has been a patient at Mayo most of his life, seeking ongoing treatment for a persistent skin condition.

"I remember going to the clinic when it was just one building. Now, it's grown so big, but the doctors haven't lost their personal touch. They spend time with you and no one rushes you along," says Mr. O'Gorman.

Now into their retirement years, the O'Gormans enjoy the life they worked so hard to achieve. Ironically though, they spend twice as much time grocery shopping as they used to. "Our son, Tim, owns the store in Hastings and our other son, Joe, owns the store in Zumbrota. The stores are 30 miles apart, but we shop at both to keep the peace," says Mrs. O'Gorman. ■

News at Mayo Clinic

Saint Marys Hospital receives national honor

Saint Marys Hospital has been awarded the Organ Donation Medal of Honor from the U.S. Department of Health and Human Services.

Representatives of 371 of the nation's largest hospitals, together with their partners in 57 organ procurement organizations, were recognized during a meeting of the Breakthrough Collaborative National Learning Congress on Organ Donation and Transplantation.

Charles Rosen, M.D., surgical director of the Mayo Transplant Center Liver Program, also received a Medal of Honor from the acting surgeon general along with the rest of the members of the collaborative faculty. The Medal of Honor is presented to hospitals and organ procurement organizations who achieve lifesaving organ donation rates of 75 percent or more for a sustained 12-month period. The national average donation rate in all hospitals was 59 percent in 2005. ■

Cancer Center SPORE grant renewed

Mayo Clinic Cancer Center's Specialized Programs of Research Excellence (SPORE) grant from the National Cancer Institute (NCI) for prostate cancer research has been renewed for an additional five years.

SPORE grants are highly competitive awards given to institutions on the cutting edge of translational research in specific types of cancer. Mayo's original five-year prostate SPORE grant of \$12 million was awarded in 2001. The current grant brings an additional \$11.2 million over five years to Mayo Clinic to advance translational research intended to reduce deaths due to prostate cancer. Donald Tindall, Ph.D., Oncology Research, is the principal investigator. ■

November 6-7, 2006: Mayo tests emergency preparedness with a flu shot clinic

Mayo Clinic held a Mass Dispensing Employee Flu Clinic November 6-7, 2006. The Mass Dispensing Clinic was designed to simulate an emergency vaccination situation. And Mayo's goal was to vaccinate a significant number of its staff as efficiently and quickly as possible. Forty dispensing stations were arranged on the Mayo Clinic Rochester campus. Over 5,700 employees participated in the two-day clinic, with one-third of those employees being vaccinated before 11 a.m. on Nov. 6. The clinic allowed Mayo to determine how well its policies and processes will help to protect staff and their families in the event of a real emergency, such as a pandemic influenza.

In addition to the influenza vaccine, the tetanus, diphtheria and acellular pertussis (Tdap) vaccine was also available. ■

Mayo Clinic Health Policy Center forum

On Nov. 13-14, 2006, the Mayo Clinic Health Policy Center assembled the first in its series of four forums at the University of Tennessee's Howard H. Baker, Jr. Center for Public Policy in Knoxville. Robert Smoldt, Mayo Clinic's chief administrative officer, and former Sen. Howard Baker hosted the event.

The two-day meeting focused on health insurance for all Americans — one of four crucial issues identified at Mayo Clinic's National Symposium on Health Care Reform earlier this year. Nearly 30 leaders from around the United States gathered to develop actionable reform solutions in a "think tank" setting. Future forums will address: improving the effectiveness and efficiency of care; increasing the integration of care; and paying for value. Forum findings will be presented at a second national symposium, which will be held near Washington, D.C., in early 2008. ■

Best friends raise funds

Best friends Claire Foussard, 10, and Ellie Fuelling, 11, both of St. Paul, Minn., know a lot about cancer and are trying to do something about it. Each of the girls has a favorite aunt who has dealt with the disease.

Sadly, Claire's aunt, Carley, passed away in January 2005 of metastatic breast cancer.

Ellie's aunt, Eleanor, is being treated for a brain tumor at Mayo Clinic Rochester.

Even though these special aunts never met, they are connected through Claire and Ellie, who say their aunts had a lot in common.

After Claire lost her Aunt Carley two years ago, the two friends decided they needed to do something to help fight cancer. They decided to raise money for cancer research.

They tried several money-raising projects. The first was a movie. They sold tickets to see a movie and staged the showing in Ellie's living room. "But we didn't raise too much money from our friends," Ellie says.

Next, they had a lemonade stand, along with the sale of other things. They made \$80 and sent the check to Mayo Clinic for cancer research.

"We considered different places to send the money," says Claire. "We decided to send it to Mayo Clinic because Ellie's aunt is getting treatment there, and it's a big place that is helping people."

With the success of the lemonade sales, they raised their business acumen and philanthropic goals up a notch.

There happens to be a place in Montana they visited this summer that Claire and Ellie say has the "best molasses cookies ever." Somehow the pastry chef was persuaded to donate the cookie recipe to the girls for their next fundraising venture.

"The recipe made a huge amount of dough," says Claire's mother, Jeanne Foussard, who helped the girls make and bake the cookies.

"The batch made 75 cookies," the girls said. They devised a sales plan the Girl Scouts of America would envy. They took orders for the cookies, and

after they baked the cookies, they wrapped the orders in foil, placed them in gift bags, tied them with ribbon and delivered the cookies on foot using a wagon — all within 24 hours. They made \$108, and a second check was sent to Mayo Clinic.

"Claire's aunt had been a financial analyst and would've loved the girls' enterprising spirit," says Mrs. Foussard.

With satisfied smiles, reminiscing about their successful endeavors, the girls say it felt good to raise money to fight cancer. "It makes us feel that we're actually making a difference," Ellie says. ■

Mayo participates in New Orleans health care relief operation

Mayo Clinic medical personnel took part in the Greater New Orleans Medical Recovery Week, Jan. 26 through Feb. 3. During their time in New Orleans, medical personnel provided health care to underserved populations in New Orleans. The event provided free medical care for Hurricane Katrina victims and residents of New Orleans who are experiencing a medical crisis and for those with unmet medical needs.

Mayo volunteers who were chosen to participate in the event were selected based on the patient needs identified by New Orleans health officials.

Following Hurricane Katrina, Mayo Clinic sent more than 250 medical volunteers and support personnel to Louisiana to help meet the medical needs of hurricane survivors. ■



Claire Foussard and Ellie Fuelling

Bold partnership confronts nursing shortage

America is facing a severe nursing shortage. In the next few years, 65 percent of nurses will retire, and the American Nurses Association predicts that by 2010, supply will be unable to meet demand. In response to this challenge, Mayo Clinic Arizona (ASU) and Arizona State University College of Nursing and Healthcare Innovation formed a partnership in 2004 to provide nursing education at the baccalaureate level.

The first graduating class of 19 students received their Bachelor of Science in Nursing (BSN) degrees on December 2006. Of this number, 14 are planning to launch their careers with positions at Mayo Clinic Arizona. The faculty for the program is composed entirely of Mayo nurses. The next class of students began classes in January.

"This exciting program with our partners at ASU will continue to contribute significantly to our ability to deliver compassionate, high-quality care to patients here in Arizona and beyond," says Victor F. Trastek, M.D., CEO of Mayo Clinic Arizona. ■

New use of targeted therapy advances treatment of early HER2-positive breast cancer

The world's first targeted therapy, trastuzumab (Herceptin), is now available for many women with early stage HER2-positive breast cancer. "This highlights a truly significant advance in the management of breast cancer," says Edith Perez, M.D., director of Mayo Clinic's Breast Clinic in Jacksonville.

Dr. Perez, who led one of the four pivotal studies that proved the drug's benefit in early stage disease, says the

approval of trastuzumab by the Food and Drug Administration (FDA) for this new use now allows physicians to manage an aggressive type of breast cancer much more effectively than just a few years ago.

It also signifies the importance for women who are newly diagnosed with breast cancer to ensure the care they will receive is the best possible, says Dr. Perez. "Women have helped lead a revolution in the care of breast cancer, and I think all patients should know all they can in order to help direct their care," she says.

"A million people are diagnosed with breast cancer in this world every year, and many are diagnosed with early disease that is potentially curable," Dr. Perez says. "This advance, and all the research continuing on novel therapies based on molecular markers in cancer, provides a brighter future for these patients."



Graduates of the Bachelor of Science in Nursing Program at Mayo Clinic Arizona.

Apart from skin cancer, breast cancer is the most common cancer in American women, and thanks to screening, more and more women are being diagnosed earlier with the disease. Breast cancer's death toll is steadily dropping. The average survival rate five years after treatment is now more than 88 percent, according to the American Cancer Society. This can be attributed to improved understanding of the disease that has led to more effective treatments. Trastuzumab is a specific type of biologic therapy, a monoclonal antibody, designed to shut down activity of these HER2 proteins by sticking to and "smothering" them, halting the pro-growth molecular instructions that these proteins relay into the body of the cancer cells. When approved by the FDA in 1998, trastuzumab helped usher in the era of targeted therapy because it specifically attacks a molecular defect on a cancer cell.

The clear benefit of adding trastuzumab to chemotherapy for patients with advanced breast cancer led Dr. Perez and other researchers to develop studies in the late 1990s. They sought to test how the drug would treat HER2-positive cancer before it had a chance to spread. They believed that if the drug could help women with the poorest prognoses, the benefit it could offer women with the earliest stages of invasive, HER2-positive breast cancer, might be dramatic. What they found was almost the proverbial magic bullet. In one of four major national studies that examined early use of trastuzumab, they discovered that the drug cut cancer recurrence by 52 percent, compared to standard therapy.

"That's the largest improvement we've seen in more than 30 years, and perhaps ever in the treatment of breast cancer," says Dr. Perez. ■

Mayo Clinic celebrates topping out of its new 214-bed, \$254.6 million hospital

Mayo Clinic recently celebrated the topping out of its new 214-bed hospital in Jacksonville. The topping out not only signals the end of the structural steel work, it also coincides with the halfway mark in the construction project. When the hospital opens in April 2008, it will integrate inpatient and outpatient services and bring its teams together in one place to do what's best for patients. Patients will benefit not only from a state-of-the-art facility, but also from the convenience, time savings, expanded resources and increased access to physicians that come with combining hospital and clinic services on one campus. To achieve this vision, Mayo launched an \$85 million fundraising effort for the hospital's construction, and, to date, more than \$81 million in gifts and pledges has been received.

The project is adding about 6,400 construction jobs for three years, increasing Mayo Clinic's economic impact on the region. The economic impact of the hospital and a separate lab construction project is estimated at \$644 million.

One of the construction industry's oldest customs, the topping-out, included the ceremonial placement of the final beam, decorated with white paint, a Mayo Clinic logo and two trees. The custom of placing a tree on a completed structure came with immigrants to the United States and it became an integral part of American culture in barn raising and housewarmings.

About the hospital:

- 214 beds, 6-floor patient tower connected to expanded Mayo Building (added three floors to existing two-story building)
- 650,000 square feet
- 14 operating rooms
- 3,900 tons of structural steel (equivalent of 2,454 Toyota Camrys)
- About 1,400 different workers have been on the project since it began
- Typical daily work force: 200
- General contractor: Centex Corp.
- Architect: Perkins+Will

For information about making a gift to the hospital, please call (800) 297-1185 or (904) 953-7200. ■



Workers place final beam of new hospital at Mayo Clinic Jacksonville.

Mayo trustees recognize new named professors

The Mayo Clinic Board of Trustees, a 30-member group of public representatives, Mayo physicians and administrators, recognized three awardees of Mayo Clinic named professorships at its quarterly meeting.

Critical care and pulmonary specialist Rolf Hubmayr, M.D., received the Walter and Leonore Annenberg Professorship in Cardiology and Critical Care in Honor of Dr. Raymond Gibbons. Dr. Hubmayr is the first recipient of this professorship, created in 2006 and funded by Leonore and the late Walter Annenberg and the Annenberg Foundation to support research in cardiology and critical care. Dr. Hubmayr, an expert in health problems related to mechanical ventilation, joined Mayo Clinic in 1984. His present research focuses on treatments that protect injured lungs from damage caused by breathing. Dr. Hubmayr is chair of the Critical Care Committee and a member of the Mayo Clinic Rochester Hospital Practice Committee.

The trustees also recognized recipients of two Walter and Leonore Annenberg Professorships in Pulmonary Medicine. These profes-

sorships were recently established by Leonore and the late Walter Annenberg and the Annenberg Foundation to support research in pulmonary and critical care medicine. The first two honorees for these professorships are:

- Andrew Limper, M.D., a pulmonary and critical care specialist at Mayo Clinic. Dr. Limper, a clinical expert in pulmonary infections, interstitial lung diseases and drug-induced lung disease, joined the staff of Mayo Clinic in 1991. His research focuses on lung infections in patients with compromised immune systems, as well as the causes and treatments of lung fibrosis. He is chair of the Division of Pulmonary and Critical Care Medicine and director of the Thoracic Diseases Research Unit at Mayo Clinic Rochester.
- Richard Pagano, Ph.D., is a consultant in Pulmonary and Critical Care Medicine with a joint appointment to the Department of Biochemistry and Molecular Biology. Dr. Pagano joined Mayo in 1994. He is internationally recognized for his research on the cell biology of lipids and its application to a number of

neurodegenerative, lipid storage disorders such as Niemann-Pick Type C disease.

Named professorships at Mayo Clinic represent the highest academic distinction for a faculty member and recognize distinguished achievement in specialty areas and service to the institution. Faculty are appointed to a professorship through nomination and endorsement of their peers and confirmed by Mayo Clinic senior leadership. ■

Mayo Clinic improves breast screening capability

Mayo Clinic's ability to find and diagnose breast cancer has increased with the addition of two new digital mammography machines, the most cutting-edge screening and detection technology available for some women.

These digital mammography machines, one a gift from The RITA (Research is the Answer) Foundation, are a valuable addition for Mayo's Breast Clinic program.

The RITA Foundation is a local, all-volunteer nonprofit organization dedicated to raising money and awareness for all cancers. The foundation emphasizes breast cancer research, awareness, education and patient programs.

"RITA is proud to have supported the breast cancer initiatives at Mayo Clinic since 2000," says Charles Jantz, RITA's founder and volunteer chair. In addition to the new digital mammography unit, valued at \$400,000, RITA's cash grants to Mayo Clinic have totaled \$165,000, which includes a recent \$25,000 commitment for mammography research.



Rolf Hubmayr, M.D.



Andrew Limper, M.D.



Richard Pagano, Ph.D.

An advance in the field of screening and diagnosing breast cancer, digital mammograms are proving to have their niche. "A large trial published in 2005 found digital mammograms have increased accuracy in three categories of patients," says Dr. Elizabeth DePeri, a radiologist in Mayo's Breast Clinic.

When compared to film mammography, digital mammography best helps those who:

- Are younger than 50 years of age
- Have dense or extremely dense breast tissue
- Are pre- or perimenopausal

FDA warns against tamoxifen use for women with CYP2D6 deficiency

A consortium of Mayo Clinic researchers and their collaborators in Indiana and Michigan recently delivered evidence to the Food and Drug Administration (FDA) that argues against tamoxifen use among a population of women who are deficient in an enzyme essential for conversion of the relatively inactive anti-estrogen to the metabolite endoxifen, which is 100 times more potent than tamoxifen.

As many as 10 percent of all women carry a genetic variant for the enzyme CYP2D6. These women have limited ability to convert tamoxifen to endoxifen. Women with the CYP2D6 variant are twice as likely to have recurrence of breast cancer if they are treated with tamoxifen for five years after surgery as are women without this specific genetic anomaly within the CYP2D6 gene.

In response to this Mayo pharmacogenetic translational research, the

FDA recommended to change the label for tamoxifen to include a warning for increased risk of breast cancer for women who are deficient in CYP2D6.

"Mayo and the NCCTG (North Central Cancer Treatment Group) were the first to show the correlation between CYP2D6 metabolism and patient clinical outcome," says Matthew Goetz, M.D., Mayo Clinic oncologist and co-leader of the study. "The label warning will include language regarding the effect of CYP2D6 metabolism. Women with genetically decreased metabolism or who are prescribed medications that inhibit CYP2D6 have a higher risk of breast cancer relapse when given tamoxifen after breast cancer."

This warning stems from the result of collaboration between numerous Mayo researchers including James Ingle, M.D., the principal investigator of the original tamoxifen study, Matthew Ames, Ph.D, whose lab coordinated all of the genetic testing, and Richard Weinshilboum, M.D., who originally suggested the hypothesis for the research project.

Currently, the target date for the label change is March 15, 2007. ■

Mayo Clinic names new chief administrative officer

Shirley Weis has been named chief administrative officer for Mayo Clinic, succeeding Robert Smoldt.

Ms. Weis has served in numerous leadership roles within Mayo Clinic, and most recently has served as chair of Administrative Services at Mayo Clinic's Arizona campus. She has also served as vice chair of Administration in Arizona; chair of the systemwide Department of



Shirley Weis

Managed Care; and executive director of MMSI. She is a member of the Mayo Clinic Board of Trustees, Mayo Clinic Arizona Executive Board and numerous other institutional committees.

As CAO, she will work with Denis Cortese, M.D., Mayo Clinic president and CEO, to coordinate overall institutional strategy and financial stewardship of Mayo resources. She also will serve as administrative vice president of Mayo Clinic and secretary of the Mayo Clinic Board of Governors.

"I am thrilled to have Shirley join our management team," says Dr. Cortese. "She brings to this position excellent strategic insight and vision; a broad perspective and experience working closely with leaders at all sites; and an excellent understanding of health care management and the health care marketplace." ■

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The Mayo Clinic Specialty Building (MCSB), featured on the cover, is a dream come true for Mayo Clinic Arizona. This state-of-the-art care facility is being funded almost entirely by benefactors who have generously contributed about \$34 million toward the project.

Certified nuclear medicine technologist

Melissa Cotton

By Suzanne Winckler

Melissa Cotton makes people smile. This is no small accomplishment when she's just asked them to eat a serving of radioactive scrambled eggs. Ms. Cotton is a certified nuclear medicine technologist at Mayo Clinic Arizona.

She dishes up the special eggs to patients undergoing a test that measures how fast food moves through the digestive tract. At two-hour intervals over the course of a day, patients return to Ms. Cotton's lead-lined room where she manages to keep them smiling while she expertly images the path of the eggs. In addition to gastrointestinal studies, she performs an array of other nuclear medicine tests that map activity throughout the body from the brain and heart to the bones and lymphatic system.

Ms. Cotton personifies the Mayo Clinic mission of providing the best care to every patient every day. She balances the very serious demands of her profession, which require constant attention to the radioactive materials she handles, with the art of keeping her patients smiling and at ease as she shepherds them through their tests. "I am a people person," she says.

She makes being a people person look easy, but exuding compassion and good humor all day long is exhausting work. Somehow, Ms. Cotton manages to conserve enough energy to be involved with Arizona Black Film Showcase, which sponsors an annual film festival and promotes black directors, producers, actors and other film-related professionals. She's also very active with the Tanner Chapel African Methodist Episcopal Church in Arizona.

Ms. Cotton credits her people skills to her father, Hershell, an executive with General Motors, and to her mother, Ethel, who is a special-needs teacher. "I always admired her gentle touch with students," she says of her mother. "My parents also exposed me to lots of different cultures at a very early age. The time we lived in Midland,



Melissa Cotton

Mich., was a great experience because professionals from all over the world lived there. My best friend was from India, and we had families from Panama, Korea and Scotland on our block. I've never been afraid of meeting people."

She loves working at Mayo Clinic because of its state-of-the-art equipment and techniques. "I like knowing the latest and the greatest about what's happening in medicine," she says. "I also love talking to people, finding out where they are from and learning all about them. My patients are my No. 1 love."



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